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or chronic, primary
or secondary
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arthritis**

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comprehensive
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salicylate alone**

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effect of low-dosage
corticosteroid¹

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plus salicylate²⁻³ brings
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restoration of function.

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including the entire
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rheumatoid arthritis

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ARIZONA MEDICINE

Journal of Arizona Medical Association

VOL. 15, NO. 3



MARCH, 1958

Original Articles

MANAGEMENT OF ACUTE RENAL OLIGURIA

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IN the past many doctors have regarded a rising or remarkably elevated NPN as a hopeless clinical situation for which further treatment is useless. With greater knowledge of renal failure and development of new techniques like the artificial kidney, such an attitude is no longer necessary. Such patients, when they have other pathological lesions should be treated specifically for those lesions, and also be given supportive therapy for their uremia. Some patients with chronic renal disease may lead an active life either attending to their business or taking care of six children with a blood NPN ranging from 70 to 120 mgm. per cent.

While the patient with chronic renal disease can only be helped temporarily by the methods now available, adequate treatment of the patient with an acute oliguria gives most gratifying results. Such patients will, if carried successfully through the acute oliguric phase, heal their renal lesion to the state of renal function existing prior to the onset of the acute oliguria. This clinical situation is usually labelled, "lower nephron

nephrosis." However, it does not seem to represent a discreet renal picture because it may have many causes and the pathological pattern at post mortem may be variable. One of the most common causes is the shock and associated anoxemia which may follow severe trauma or surgery. Next in order of occurrences are the acute hemolytic diseases, and the toxic nephroses which may follow exposure to carbon tetrachloride, bichloride of mercury, bromate, ethylene glycol or other toxic agents. Acute oliguria may also occur in association with acute respiratory infections such as bronchopneumonia¹. In addition there are other causes of acute oliguria which do not seem to fall in the above categories, as for example, the oliguria of hypo- or hypernatremia, that of acute nephritis and that sometimes associated with subacute bacterial endocarditis. The patient with chronic renal disease who develops oliguria following an infection, surgery or an accident will also be considered in this paper because the clinical management is identical even though the pathological picture and ultimate prognosis may be different. The acute oliguria following overdosage with sulfadiazine may represent a special type of oliguria which is considered secondary to extensive precipitation of crystals in the renal tubules. Furthermore, treat-

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**The author wishes to acknowledge the help of all members of the hemodialysis team, and particularly, Dr. Peter Van Schoonhoven, Dr. William Robb, Dr. Theodore Richey, Dr. George Mami, Dr. William Takenda and Dr. Thomas Hickman. Supported in part by the Mary B. Flynn and Mrs. Coming Benton Funds.

ment is different because immediate hemodialysis may lower "sulfa" blood levels to a point where further renal damage is kept to a minimum.

In many instances the exact reason for the development of lower nephron nephrosis is not clear. We accept readily enough the explanation of renal anoxemia secondary to the severe shock and severe hemorrhage following, for example, a hysterectomy^{2,3}. In contrast the patient undergoing a simple appendectomy with no obvious drop in blood pressure throughout the operative period and not requiring any transfusions who suddenly developed an acute oliguria, presents a much more perplexing problem. An equally perplexing problem is the occurrence of acute oliguria following a "flu-like" infection or a broncho-pneumonia¹. This problem has not been elucidated by animal studies since no consistent method for the production of lower nephron nephrosis has yet been devised. Table 1 shows the incidence of shock, administration of blood, transfusion reactions and other factors believed responsible for causing lower nephron nephrosis in all the patients with acute oliguria treated by dialysis at Colorado General Hospital up to March 1957. While the exact cause of the acute oliguria may not be apparent in every instance, the management of these cases is identical.

The treatment of a case of acute oliguria which follows surgery can be divided into three phases, the initial period covering the first 24 to 48 hours, the remaining period of oliguria, and the diuretic phase. In the initial phase the primary therapeutic objective is the treatment of the cause. This may include adequate and prompt restoration of blood volume in the case of shock, symptomatic treatment of the transfusion reaction and administration of sodium bicarbonate, and in the case of acute nephrotoxins, removal of these agents either by dialysis or exchange transfusion if that seems feasible. For example, recently a patient received 50 gms. of sulfadiazine intravenously. This patient was immediately put on the artificial kidney. The original sulfadiazine level in the blood exceeded 80 mg. per cent. At the end of the dialysis period it was lowered to a value of 20 mg. per cent. Ureteral catheters were also passed to make sure that precipitation of sulfadiazine crystals had not blocked the ureters. The patient responded well

and had only a short period of oliguria lasting four to five days. He then started putting out large volumes of urine, and subsequent dialysis was not needed. If there is any doubt that the ureters are blocked in any of these cases this should be checked immediately. Cystoscopic examination is indicated when the patient is not excreting any urine.

TABLE 1
ETIOLOGY OF ACUTE ANURIA
(Hemodialysis - 15 Cases)

Shows the possible etiologic factors in the last 15 patients with acute oliguria or lower nephron nephrosis which were sent to this hospital for dialysis.

Surgery	9	Blood Transfusions	6
Trauma	2	Incompatible Blood	2
Shock	7	Acute Glomerulonephritis	2
Carbon Tetrachloride			

Following the initial period the patient then passes into a phase of prolonged oliguria which may last anywhere from four to over 20 days with an average of about eight to 10 days. Our record case was oliguric for 29 days. Good management during this phase is particularly important. Let us consider some of the important features of conservative therapy.

While an indwelling catheter is most comforting to the physician and allows him to make frequent measurements of the urinary output, it often produces a cystitis. Thus, where possible it may be best not to use an indwelling catheter.

Perhaps one of the most important aspects of therapy in these cases is the administration of fluids. Years ago these patients were given too much fluid, sometimes in the hope of initiating diuresis. A carefully kept intake and output record is most important in following these cases. The daily fluid requirement should include the previous day's output (urinary or other losses) plus an allowance for insensible water loss - usually about 700 to 1,000 cc. per day. This latter figure may vary with conditions, for example, in summer more fluid is required than in winter, and if the patient sweats, an additional fluid loss must be estimated. It seems ideal to keep the patient mildly but not severely dehydrated. In the latter case there appears to be an increased danger of pulmonary and salivary gland complications resulting from the markedly thickened secretions. When the patient continually complains of severe thirst, the mouth is completely dry, and he is unable to swallow adequately because of lack of saliva, then probably more fluids are indicated. Measurements of salivary flow by the mouth breathing tech-

nique have been made in many of these patients and have proved useful in quantitatively evaluating the dryness of the mouth. It is not sufficient to order the daily fluids in the morning. One must check at least several times daily to determine if the patient is getting what was ordered that morning and also whether the fluid exchange has changed due to increased urinary output, diarrhea or vomiting. The patient should be weighed daily. According to Merrill(2) a patient on intravenous fluids, with no food by mouth, should ideally lose about .3 kilogram body weight per day.

Where possible we try to keep these patients eating food by mouth throughout their hospital course. The diet prescribed is a low protein, high carbohydrate, high fat diet designed to supply sufficient calories as carbohydrate and fat so that metabolism of protein is kept to a minimum. This tends to prevent a rapid rise in the blood NPN and creatinine. This diet is also low in sodium and potassium. It is not an attractive diet but many patients eat it well. The strictest diet used has only 20 gms. of protein per day. When it is possible, as diuresis starts, to raise the protein content to 30 gms. per day and permit salt, then the diet is much more attractive. The use of butter balls and butter soup have been disappointing in our experience since they produce nausea and gastrointestinal discomfort so that very few patients will tolerate them. When continued intravenous therapy is required calories can be supplied by intravenous fat and glucose solutions. In a patient with hemorrhage into the peritoneal cavity or severe trauma the NPN may rise as rapidly as 30 to 60 mg. per cent per day. In the average uncomplicated case on a low protein diet this increase can be kept to a minimum of less than 20 mg. per cent per day. An anabolic agent like testosterone may also be useful in preventing a rapid rise of the NPN. This is usually administered as 25 mg. of the propionate given three times a week for several weeks(3) or daily for a maximum of 10 days(2).

Another important aspect of therapy is the control of the electrolyte concentrations in the body fluids. The usual electrolyte changes during the period of oliguria are a decrease in the serum sodium and chloride concentrations, a rise in the serum potassium, a decrease in the serum bicarbonate, an elevation in the serum

phosphate, and no change or a slight drop in the serum calcium. The serum magnesium may be elevated but as yet little clinical significance is attached to this change. Serum proteins usually do not change. However, in an occasional case there is a significant decrease in their concentration, and one should then look for concomitant liver damage. The organic acid concentrations in the serum which are not measured directly presumably increase and the extent of their rise is indicated by the rate of decline in the serum bicarbonate. The decrease in serum concentrations of sodium and chloride should be treated only if there are significant changes such as a sodium below 133 meq/L or a chloride below 92 meq/L. When the serum bicarbonate is relatively normal, our choice of solutions for restoring the serum sodium and chloride concentrations is usually five per cent chloride administered intravenously but given very slowly. The method used for calculation of the initial dose is 140 (ideal serum concentration) minus the actual serum sodium concentration in meq. times 25 per cent of the body weight in kilograms (this represents the extracellular volume). The serum sodium and chloride concentrations are again checked the next morning and if a sodium deficit still exists further salt is given using the same method of calculation. Usually after such therapy there will be a distinct improvement in the patient's clinical condition. Salt replacement is considered more urgent in the presence of a falling blood pressure. However the five per cent sodium chloride solution must be given slowly (200 cc. in six to eight hours) and in the presence of cardiac failure and edema the patient watched carefully to prevent pulmonary edema. When the serum bicarbonate is low then up to one third of the total sodium replacement should be given as sodium lactate or bicarbonate solutions.

Changes in the patient's serum potassium concentration may represent a serious threat to life. Serum potassium concentrations approaching eight meq/L may cause major changes in the electrocardiogram, heart block and eventual death.(8, 9) There are several conservative methods which may prove valuable in preventing significant elevation in the serum potassium. First is the intravenous administration of hypertonic glucose solutions and insulin. The insulin is usually added to the infusion fluid at the rate of one unit for each two to four grams of glucose.

The concentrations of glucose solution used may range from 10 to 25 per cent and the daily amount administered is limited to the total quantity of fluids calculated for the specific patient.(5) While the more concentrated solutions may be somewhat more effective they also are more likely to produce thrombosis and phlebitis. When glucose is stored in the tissues as glycogen, potassium and water also enter the cells thus reducing the serum potassium. It is well established that potassium will tend to leave the cells in the presence of an acidosis associated with a drop in the serum bicarbonate and tend to re-enter the cells when the serum bicarbonate is raised or an alkalosis is induced.(4) Therefore in patients with acute oliguria when the serum sodium and bicarbonate concentrations are reduced, administration of sodium bicarbonate offers a good method for lowering or controlling the serum potassium concentration. The usual preparation of sodium bicarbonate comes in 50 cc. ampules, containing approximately 40 mEq. of each. This can be added to the 10 per cent glucose to give a replacement calculated in the same manner as described previously for sodium. In our experience sodium bicarbonate is preferable to sodium lactate because if the patient has associated liver damage the lactate may not be metabolized and further increases the serum concentration of organic acids. Another method frequently employed for control of the serum potassium is the use of cation exchange resins either in the ammonia or sodium form. When used these resins should be started early in the oliguric phase. They can be administered either by mouth or by rectum as a retention enema. In the latter case one mixes 50 gms. of resin with approximately 100 to 150 cc. water in the barrel of an asepto syringe and then immediately introduces the mixture into the rectum. In some cases the serum potassium has apparently been kept under control by use of these materials; on the other hand they have proved constipating and frequently cake in the rectum when given in that form. Once the serum potassium reaches dangerous proportions (above 7.5 mEq/L) the above methods are rarely effective in reducing it immediately. The only method offering any hope is that of hemodialysis.

Significant early changes in the electrocardiogram produced by a rising serum potassium include increase in amplitude and peaking of the

"T" wave. When changes in conduction occur, the prognosis is limited and immediate hemodialysis is indicated. These changes may include prolongation of the PR interval up to a Wenkebach's phenomenon, spreading of the QRS complex and bundle branch block. The extreme changes noted in the electrocardiogram shown in Fig. 1 occurred in a patient who had a serum potassium of 9 mEq/L. Unfortunately there was a delay in transferring this patient to our institution, and he died in shock before he could be put on the artificial kidney. Many clinicians have dropped the routine use of calcium salts in therapy of oliguria unless obvious tetany is present because it masks the recognition of the symptoms and EKG changes of hyperkalemia. However, until the patient can be put on the artificial kidney, administrative of calcium gluconate intravenously as a slow drip will frequently reverse the potassium changes observed in the EKG and eliminate temporarily the heart block. Calcium gluconate comes in 10 per cent solution, 10 cc. per ampule and can be given up to maximum doses of 100 cc. in a constant drip infusion spread over a 24 hour period.(8,9) This procedure is usually not effective for more than 12 to 24 hours, but this provides time for transferring the patient to an artificial kidney.

Initially when the serum potassium reaches concentrations of eight to nine mEq/L and the

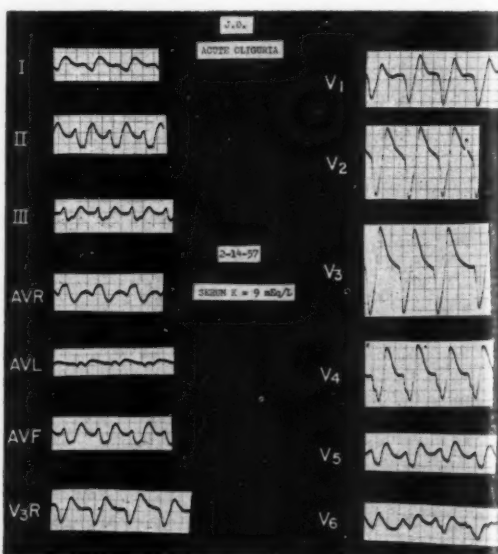


Fig. 1

EKG shows only a sine wave pattern (See Fig. 1) the patient feels so well that many clinicians procrastinate about putting the patient on the artificial kidney. Suddenly the patient gets much worse and dies within a matter of minutes. Digitalis should be avoided at this time, especially if use of the artificial kidney is contemplated because as the serum potassium is reduced appreciably during dialysis, the digitalis effect becomes exaggerated and may produce heart block and ventricular premature beats. EKG changes as severe as those noted in Fig. 1 will revert to normal within 45 minutes after hemodialysis is started.

Antibiotics should be avoided unless specifically indicated. We never use streptomycin because of its possible nephrotoxic effect and because it may change markedly the normal flora of the GI tract. Most antibiotics are excreted by the kidney and in some instances, as for example, penicillin, the excretion is quite large. Therefore in an oliguric patient a smaller dosage of antibiotic can be used. In the case of penicillin, doses of 400,000 to 600,000 units daily will maintain a high blood level in these patients. Furthermore, since there is no renal loss of the antibiotic one injection a day will maintain high blood levels throughout the 24 hour period. Precise dosage for the other antibiotics in patients with oliguria are not available but one would suggest that a dosage from 50 per cent to 75 per cent of the normal dose would be more than adequate. Permitting the patient to eat as long as possible and be up and around or sitting in a chair has, in our opinion, proved particularly useful in preventing respiratory and abdominal complications.

Convulsions, when they occur, are particularly disconcerting. Three types of therapy have been used for their control. When the blood pressure is excessively high, a large dose of intravenous rauwolfia has proved very useful. Barbiturates are used, particularly sodium luminal or phenobarbital because if the artificial kidney is to be used, phenobarbital will dialyze out much more readily than seconal for example and the "hang-over" effect will be eliminated. Magnesium sulfate has also proved useful but has been given rather empirically. Some of these cases have an elevated serum magnesium (up to three to four meq/L), and one wonders whether the administration of further magnesium might be wise. The patient should be checked continually

for respiratory complications, and these should be treated symptomatically. For example, bronchoscopic examination should be done for the mucous plugs and atelectasis, antibiotic therapy employed for pneumonia, and pressure breathing and morphine used for pulmonary edema. When the patient is kept extremely dry and has no salivary secretion, infections of the parotid gland do occur and these glands should be checked frequently.

When the urine volume begins to increase it usually increases gradually for the first four to six days. For example, the daily urine volumes may be successively 100 cc., 200 cc., 275 cc., 350 cc., 450 cc., and 600 cc. Suddenly the urine volume will start to increase rapidly and every eight hour period of urinary output will exceed the preceding one until the daily volume reaches four to 10 liters. During this phase of maximum diuresis there are two important features of therapy: 1) The treatment of any infections which appear and 2) replacement of the electrolyte loss occurring through the urine. Respiratory complications or convulsions may occur frequently during the early part of the diuretic phase. The blood NPN does not drop immediately and may even continue to rise for several days after the onset of maximum diuresis. At this time the kidneys are putting out a dilute urine with fixed concentrations of sodium, potassium and chloride. These electrolyte losses can be quite large as were observed in the three patients presented in Table 2. On the basis of the urinary losses shown in the table, in order to replace only the sodium chloride, the first patient would require the equivalent of six liters of .9 per cent saline daily, the second three liters and the third 1.8 liters. Thus if these patients are not followed carefully a severe

TABLE 2

Shows for a single 24 hour period the urinary volume and total excretion of sodium potassium and chloride in three patients during the diuretic phase following acute oliguria (lower nephron nephrosis) a liter of 0.9 per cent saline contains 154 meq. of sodium.

Patient	Electrolyte	Urine Vol: L.	Conc. meq/L.	Total meq/24 hour
J.P.	Na	14.2	70	995
	K		12.6	179
	Cl		69.6	989
F.C.	Na	7.2	64.8	472
	K		36	261
	Cl		69	505
E.A.	Na	2.2	117	258
	K		25	55
	Cl		98	217

hyponatremia or hypokalemia may occur. The best replacement procedure is to determine the electrolyte concentrations of the urine in each case and then replace the calculated losses daily. Usually this can be done orally and Patient "J.P." in the chart would drink as requested four to six liters of Ringer's solution daily instead of water. If frequent urinary electrolyte determinations are not possible a single study of the concentrations in a 24 hour urine will be sufficient. These concentrations can then be multiplied by the daily urine volume and replacement on subsequent days can be based on these figures. While this will not give a precise replacement, it will be sufficiently adequate for therapy in over 90 per cent of the cases.

The artificial kidney has now been developed beyond the experimental stage and with new equipment, namely the Kolff Twin Coil replaceable unit(5, 6) has now become a treatment to be used when indicated just like any surgical procedure. It should be used in conjunction with the treatment outlined above and not resorted to as a last desperate measure when everything else fails. The patient's blood is pumped from a polyethylene catheter inserted either in the radial artery or in the vena cava and then passed through two cellophane tubes, each 10 meters long which are interposed between layers of the fiberglass window screen. Blood flows through these tubes at the rate of approximately 200 to 300 cc. per minute. Wash solution is passed over the window screening at a rate above five liters per minute, thus making it possible for exchange of diffusible solutes to take place between the blood and the wash solution. Exchange can take place in either direction. Thus, if it is desired to remove solutes from the blood their concentration is kept at low or zero levels in the wash solution. If it is desired to transfer solutes from the wash to the blood, concentrations are maintained at higher levels in the wash solution. For example, a patient with a sodium concentration of 124 mEq/L (normal 140 mEq/L) would be dialyzed with a wash solution containing approximately 148 mEq. of sodium. Actual measurements initially showed that while the blood entered the artificial kidney at a sodium concentration of 124 mEq/L., it was returned to the patient at a concentration of 138 mEq/L. As this process continued the patient's serum sodium concentration would be gradually restored to normal. It is also possible

to remove large volumes of water in the edematous patient or the patient with acute cardiac failure. This is accomplished by raising the osmotic pressure of the wash solution through the addition of glucose and by increasing the hydrostatic pressure in the dialysis unit. During an eight hour dialysis we have removed as much as 14-18 pounds of fluid.

It requires approximately 800 cc. of citrated blood to fill the dialysis unit initially. We usually order four to five pints so that if the patient requires additional blood, it is available. If the unit is filled properly with blood there will be no change in blood volume during dialysis since blood is taken from the patient and returned to him at equal rates. The patient must be heparinized usually at the rate of one mg. heparin per kilogram of body weight. Ten mg. of heparin are also added to each bottle of bank blood used. There is the possibility that the heparinization will initiate bleeding. However, cases have been treated where the patient was bleeding prior to dialysis and after the first two hours of dialysis, stopped bleeding. Therefore, we do not consider hemorrhage in a patient as a contraindication to dialysis. When the dialysis is completed the remaining heparin is neutralized with protamine sulfate.

The operation of the kidney requires a team of five people, two physicians, a nurse, a laboratory assistant and a medical technologist. Initially blood chemistries were done every two hours during the dialysis. As the team gained experience these could be reduced to a minimum of three blood chemistries for an eight to 12 hour dialysis. The wash solution is changed every hour during the first four hours of dialysis and every two hours thereafter. The composition of the wash solution designed specifically for each patient is changed throughout the dialysis according to the results of the repeated chemical analyses. Thus in most patients by the end of an eight to 10 hour run it is possible to restore the chemical constituents of the blood to normal except for the elevated NPN which will be markedly reduced — perhaps to a minimum of 60 mg. per cent.

Fig. 2 shows the Kolff twin coil dialysis unit in operation. The stainless steel tub contains the 100 liters of wash solution which is circulated over the coil unit in the center by a water pump mounted underneath the tub. The blood from



Fig. 2. Shows the Koff twin coil dialysis unit in actual operation at the Colorado General Hospital.

the patient's radial artery is pumped through the cellophane tubes in the coil by the sigma motor pump located on the right side of the tub. Steel fingers in the pump propel the blood by squeezing on the plastic tubing. After leaving the coil the blood passes through the "bubble catchers" hanging from the steel stand and then by gravity flow returns to the patient's vein. A heating coil and thermostat maintain the temperature of the bath solution. The scales and chemicals used for making the wash solution are shown. Oxygen and CO_2 are passed through the wash solution in order to oxygenate the blood and to maintain the pH of the wash solution.

The accompanying table,(3) shows the changes in blood chemistry which can be achieved in an eight hour dialysis in a typical patient with uremia. The NPN dropped from 200 mgm. per cent to 50 mgm. per cent and blood creatinine from 18.5 mg. per cent to 5.9 mgm. per cent. The reduced serum sodium and

TABLE 3

Shows the changes in blood chemistry produced by eight hours of hemodialysis in a patient with chronic glomerulonephritis. This patient, a white male, age 51, had been able to work for the past several years despite an elevated NPN of approximately 100 mgms per cent. He had a convulsion and was dialyzed that evening with the results noted below.

	0 Hours	8 Hours
NPN	200.0 mgm. %	57.0 mgm. %
K	4.4 meq/L	3.3 meq/L
HCO_3	10.8 meq/L	29.0 meq/L
Creatinine	18.5 mgm. %	5.9 mgm. %
Na	134.9 meq/L	148.0 meq/L

bicarbonates were raised to values at the upper range of normal.

The indications for dialysis are sometimes difficult to standardize. We have used the following four criteria: 1) when the serum potassium rises above 7.0 meq/L.; 2) when the carbon dioxide combining power drops below 10 meq/L.; 3) when the NPN rises above 200 mgm. per cent; and 4) when the patient develops the toxic signs of uremia. Hyperpotassemia is the most critical factor for life and in the early days of the artificial kidney several patients died because dialysis was not started earlier. As mentioned previously when the EKG

shows serious changes, one can anticipate a maximum life expectancy of 24 hours without dialysis. Dialysis will promptly reduce serum potassium concentrations to levels of approximately three mEq/L. A carbon dioxide combining power of 10 mEq/L is extremely low and is frequently associated with respiratory distress which can be relieved by dialysis. The NPN or BUN is not strictly indicative of the degree of toxicity. Some patients will manifest no toxicity when the NPN is up to 300 mgm. per cent. We have adopted the policy however that when the NPN gets above 200 mgm. per cent then dialysis is definitely indicated in the majority of patients. A very important indication is the clinical condition. When any signs of toxicity, such as drowsiness, mental aberrations, nausea and vomiting or approaching coma appear, dialysis is performed. In this way the patient is kept alert and feeling well throughout the course of oliguria. In our opinion this policy has proved effective in preventing many complications such as convulsions, respiratory infections, etc. It also shortens remarkably the period of convalescence. Even though the patient may be starting to give evidence of diuresis, dialysis is repeated if any of the above indications are present. In our opinion the infections and other complications encountered in these patients are minimized if a good clinical condition is maintained and the blood chemistries are kept within

reasonable ranges. For this reason, patients with anuria should be transferred early to centers where an artificial kidney is available. Thus they can be followed carefully and whenever dialysis is indicated it can be done promptly. If the artificial kidney is used as an elective procedure and not as a last resort measure, then we feel many more lives will be saved among the uremic patients.

Table 4 shows all the patients dialysed by our unit because of acute oliguria following trauma or surgery up to March of 1957. It shows the type of surgery or injury preceeding the oliguria, number of dialyses required, the NPN and carbon dioxide combining power before and at end of dialysis. The probable cause for the oliguria for this series of patients is shown in Table 1. The term recovery indicates complete recovery. In many of the fatal cases the dialysis was satisfactory, but the patient died during the diuretic phase of complications such as acute cholecystitis, atelactasis, pneumonia or septicemia. The deaths due to septicemia and pneumonia were caused by organisms resistant to the usual antibiotics. Perhaps some of these deaths could have been prevented by earlier and more frequent dialysis.

The artificial kidney also has two other important uses which will be mentioned briefly. Excellent results are obtained by the rapid removal of accidentally ingested toxic materials which are

TABLE 4
ACUTE OLIGURIA (Lower Nephron Nephrosis)

Shows the cases of lower nephron nephrosis following trauma or surgery which were treated by dialyses at Colorado General Hospital through March, 1957. It gives a general picture of the age grouping, number of dialyses required, type of injury or surgery, results and the pre-dialyses and post-dialyses, NPN and CO-2. Those cases marked with an asterisk were done on the Skaggs Leonard unit, the others on the Kolff twin coil disposable unit.

Patient	No. of Dialyses	Age	Surgery or Injury	NPN mgm.% Before	After	CO-2 — meq/L Before	After	Outcome
*M.M.	1	35	Hysterectomy	260	132	16	26	Died
*R.P.	1	42	Multiple fractures	190	122	15	28	Recovery
*H.H.	1	33	Repair atrial septal defect	250	190	9	19	Died
*L.A.	1	25	Cesarean section	325	190	17	19	Died
*F.R.	1	28	Multiple fractures, head injury	214	166	17	19	Died
*G.M.	1	59	TUR (Prostate)	230	—	11	22	Died
H.B.	1	63	Nephrectomy	142	60	17	25	Died
H.B.	3	53	Aorticthrombosis-Nephrectomy	230	105	19	26	**Satisfactory
W.B.	3	62	Prostatectomy	123	71	8	20	Recovery
R.L.	1	19	Trauma, head injury	240	108	18	28	Recovery
C.P.	1	29	Appendectomy	199	96	18	26	Recovery
A.C.	2	49	Hysterectomy	263	116	14	25	Died
A.E.	1	60 plus	Hip Fusion	178	108	16	19	Died
E.L.	1	47	Cholecystectomy	250	126	10	20	Died
I.M.	1	58	Hip prosthesis	108	62	20	34	Recovery
D.N.	1	21	Fracture left femur	243	136	14	22	Recovery
O.H.	1	79	Prostatectomy	214	80	14	25	Recovery
E.M.	3	70	TUR (Prostate)	193	84	18	24	Died
E.V.	2	37	Hysterectomy	198	68	9	21	Home

**Death after third dialysis due to improper medication

capable of passing across the cellophane membrane.(10) Thus the patient with acute barbiturate poisoning may be brought out of coma in a matter of eight hours. Recently a patient with Doriden intoxication responded in a similarly gratifying manner. Salicylates, bromide and methyl alcohol are also effectively removed. Hemodialysis has also proved useful in the management of chronic renal disease. It's usefulness seems limited to those cases where it is known that the patient can put out a good urine volume, and thus maintain the improvement achieved initially by the artificial dialysis. Some patients have even returned to work for as long as two to six months after dialysis. A patient with chronic renal disease who develops an infection or requires surgery is an excellent candidate for dialysis with the artificial kidney as a supportive measure to carry him over the acute emergency.

SUMMARY: Great strides have been made in the treatment and management of the oliguric patient, and as a result the mortality in this group has been markedly decreased. The essential features of conservative therapy include balanced administration of fluids, low protein

high caloric diet, proper restoration of abnormal electrolyte concentrations, control of the serum potassium levels by the methods outlined and good symptomatic therapy. The artificial kidney offers a technique which has proved useful in managing many types of problems with oliguria and acute uremia. It's early use as an elective procedure to keep the uremic patient in excellent condition was advised.

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THE ARTIFICIAL KIDNEY

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WITH THE availability of an artificial kidney in Arizona* there is need for a brief review concerning its use. Three cases recently treated with the artificial kidney are presented.

The presently available machine is the Kolff disposable coil type kidney(1,2) shown in Fig. 1. Arterial blood, usually obtained from the patient's radial artery, is pumped by the sigma-motor pump (E) into the cellophane tubing (B). Here the blood in the cellophane tubing comes in intimate contact with the bath fluid (C) and dialysis through the semipermeable cellophane takes place. The blood is then passed through a filter (F) and back to the patient through one of the large arm veins. The bath fluid (C) is circulated through the cellophane coil by means of a pump. The contents of the bath are shown in Fig. 2. The bath is maintained at constant temperature with a thermostatically controlled heating rod. Oxygen with 10 per cent carbon dioxide (D) is bubbled into the bath to maintain the pH. The dialysis lasts five to six hours with changes of the bath fluid every two hours. The blood of the patient is heparinized. Blood flow through the machine is maintained at 200-400 ml. per minute.

Case I. M. L. A 39-year old Mexican American female with no prenatal medical care was admitted to Memorial Hospital on June 20, 1957, in a semi-stuporous state, for delivery of her eighth pregnancy. A history of untreated diabetes was elicited and a 50 ml. catheterized urine specimen revealed four-plus sugar. A diagnosis of diabetic acidosis with incipient coma was made. In the next six hours, the patient received 1,000 ml. whole blood, 1,750 ml. normal saline, and 220 units regular insulin parenterally. The blood sugar fell in 12 hours to 76 mg. per cent. At this time, the patient delivered a dead, full-term, unmascerated fetus. The blood sugar soon after delivery was 42 mg. per cent and the patient was perspiring profusely. She was given hypertonic glucose which terminated the hypoglycemia. A few hours after admission the patient was found to be anuric. (See Fig. 4.) During the first six hospital days, the

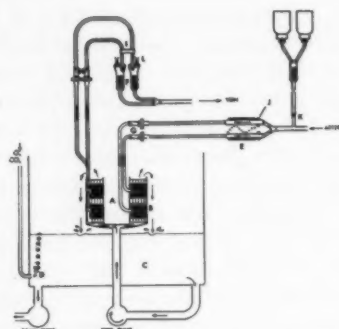


Fig. 1. Schematic diagram of the twin coil disposable artificial kidney.

Composition of Rinsing Fluid for Artificial Coil Kidney

Component	Gm./100 L.	mEq. L.					
		Na ⁺	K ⁺	Ca ⁺⁺	Mg ⁺⁺	Cl ⁻	HCO ₃ ⁻
NaCl	570	97	—	—	—	97	—
NaHCO ₃	300	36	—	—	—	—	36
KCl	40	—	5	—	—	5	—
CaCl ₂	28	—	—	5	—	5	—
MgCl ₂	15	—	—	—	3	3	—
Total		133	5	5	3	110	36

Invert sugar (Travert) 0.4 per cent.
Lactic acid to adjust pH to 7.4.

Fig. 2.

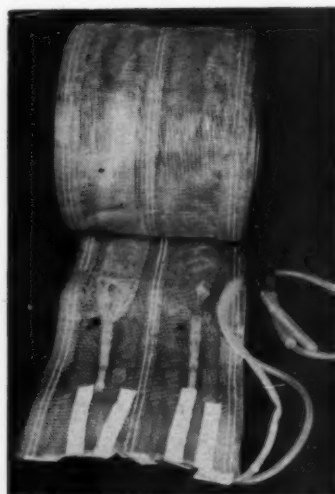


Fig. 3. Stationary disposable coil with 2 tubes of cellophane coiled and separated by fiberglass screen.

*St. Joseph's Hospital, Phoenix

**Copied from drawing made by Travenol Laboratories, Morton Grove, Illinois

*Sodium polystyrene sulfonate resins supplied by Winthrop Laboratories.

patient's status remained fairly stable. There was a gradual rise in serum potassium from 5.4 to 6.0 meq./l. The blood urea nitrogen slowly rose from 20 mg. per cent to 88 mg. per cent on the seventh hospital day. The blood sugar was readily controlled by small doses of regular insulin. Fluid intake was restricted to 500 ml. of fluid per day and oral feeding for this purpose consisted of a high caloric glucose-olive oil mixture (Bull diet). Despite the administration of 3,000 ml. whole blood, the hematocrit rose from 18 per cent to only 25 per cent during the first week. On the seventh hospital day, 50 ml. of urine was obtained, the first urine since admission. The patient then developed pulmonary edema following pulmonary embolism which responded to treatment with morphine, Digoxin, tourniquets, and oxygen. On the ninth hospital day, bradycardia and shock occurred when the serum K level was 8.4 mg. per cent. EKG showed a bradycardia, widening QRS to 0.16 seconds and very wide T waves, diagnostic of potassium intoxication (see Fig. 5). The patient was given calcium, hypertonic glucose and insulin intravenously, following which the blood pressure rose to 140/90; the pulse rate rose to 100 beats per minute. A repeat EKG showed reversion of the above changes to normal. After this emergency treatment for potassium intoxication, the patient was transferred to St. Joseph's Hospital for emergency dialysis with the artificial kidney. The first artificial kidney dialysis was performed on the ninth hospital day for six hours, during which the BUN fell from 113 to 41 mg. per cent and the serum potassium from 8.4 to 6.0 meq./l. The patient was then maintained on oral fluids not exceeding 500 ml. per day above the measurable water loss. The urine output remained less than 100 ml. per day. Sulfonate ion exchange resins*** were administered rectally from the 13th to the 20th day and seemed to control the serum potassium (see Fig. 4). On the 21st hospital day, artificial kidney dialysis was performed for the second time because of uremic intoxication. During dialysis the BUN dropped from 145 mg. per cent to 70 mg. per cent. During the following week, the patient appeared to improve. The urinary output exceeded 500 ml. for the first time on the 24th day. The output increased steadily and reached a peak of 1,250 ml. on the 29th day. Thereafter, there was a gradual decrease in urinary output: the total on the

34th day was 600 ml. During this period, the serum potassium dropped to levels below 3 meq./l. and parenteral potassium was required. The BUN rose from 100 mg. per cent on the 29th day to 165 mg. per cent on the 34th day. During this time, the patient again developed increasing uremic intoxication. A third artificial kidney dialysis was attempted on the 35th hospital day. Due to technical difficulties in can-

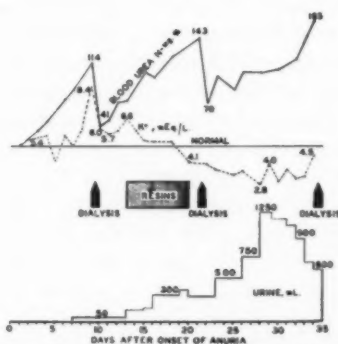


Fig. 4 Case 1. M.L. A woman with postpartum anuria and diabetes. Artificial kidney dialysis performed three times. Diuresis started but was not maintained and patient died on the 35th day. Autopsy revealed eclamptic renal changes and findings associated with Kimmelstiel-Wilson disease.

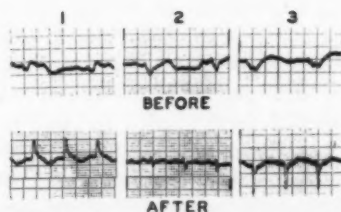


Fig. 5. Case 1 M.L. Above: 3 leads I, II & III taken at time serum potassium was 8.4 meq./l. Below: Leads I, II & III taken 15 minutes later following administration of intravenous calcium gluconate, glucose and insulin.

nulating the arteries and veins, an adequate dialysis could be maintained for only two hours. While an effort was being made to insert canulas into different locations, the patient suddenly went into shock. An EKG showed ventricular tachycardia which progressed to ventricular fibrillation and death despite treatment with intravenous procaine amide.

At autopsy, the pathologic changes were limited to the kidneys. Grossly, the cortices of both kidneys were very thin, approximately one-third normal size. The cortices were yellow, yet not necrotic. Microscopically, the renal lesions of eclampsia and Kimmelsteil-Wilson disease were found.

Comment: This case demonstrated that the effect of intravenous calcium, hypertonic glucose and insulin on the symptoms and electrocardiographic changes, of severe hyperkalemia, is immediate and striking, and in this case permitted adequate time to transfer the patient from one hospital to another for emergency dialysis. The use of the new sulfonate ion exchange resin per rectum appears effective in lowering the level of serum potassium and may at times prevent the necessity for dialysis for potassium intoxication. The gradual diminution of urinary output after beginning diuresis is unusual. It is possible that the acute eclamptic changes in the kidneys were reversible but the Kimmelsteil-Wilson changes were not reversible and became worse.

Case II. J. B. A 33-year old white male was admitted to St. Joseph's Hospital for emergency artificial kidney dialysis on Nov. 5, 1957. An orthopedic procedure was successfully performed in a neighboring city on Nov. 2, 1957. Shortly after completion of the operation, he was found to be in profound shock. After approximately 30 minutes of severe hypotension, he became normotensive with the administration of whole blood transfusions. Post-operatively, he became severely oliguric and produced 50 to 100 ml. of urine daily. During the two days prior to transfer to St. Joseph's Hospital, the BUN increased from 52 to 170 mg. per cent; the serum potassium rose from 6.2 to 8.2 meq./l., and the CO_2 dropped from 18 to 9.9 meq./l. An electrocardiogram showed definite evidence of potassium intoxication (tall, peaked T waves, prolonged P-R interval, slight widening of QRS in chest leads). On the basis of these findings, artificial

kidney dialysis was begun immediately and continued over a five-hour period. Changes in serum potassium and blood urea nitrogen correlated with the dialysis and the ensuing diuresis are shown in Fig. 6. The patient was discharged from the hospital 21 days following onset of anuria, asymptomatic save for slight residual nausea.

Comment: Emergency dialysis was performed on this patient for the purpose of lowering the serum potassium, which had reached dangerously high levels. This was successfully accomplished.

Case III. L. H. A 30-year old white carpenter suffered severe electrical burns involving the left arm, trunk and right leg, due to the accidental grounding of a high tension wire on Nov. 2, 1957. He was brought immediately to the hospital and found to be severely oliguric after passing some wine-colored urine. After the initial shock, the patient was normotensive. He received 1,000 ml. whole blood, 100 ml. serum albumin and 6,700 ml. intravenous electrolyte fluids during the first three days. He was disoriented during the first 36 hours and then gradually became comatose. A guillotine type amputation of the left arm at the shoulder was performed on the fifth post-injury

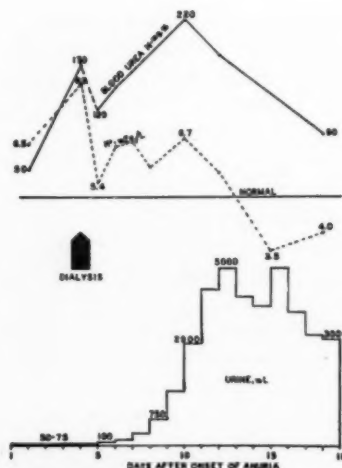


Fig. 6. Case 2, J.B. A male with post-operative shock who developed renal shutdown and serious potassium intoxication. Artificial kidney dialysis promptly returned the blood potassium to safe level.

day. The BUN gradually rose from 75 mg. per cent to 242 mg. per cent. The oral and rectal sulfonate ion exchange resins seemed to control the serum potassium (see Fig. 7). Artificial kidney dialysis was performed on the sixth post-injury day because of uremic intoxication. The dialysis was complicated by bleeding from the amputation stump. A tracheotomy was performed on the eighth post-injury day. Because of marked acidosis and uremia, artificial kidney dialysis was performed for the second time on the eighth post-injury day. Marked fever developed at this time with temperature ranging 102 to 105 degrees. Plans for kidney dialysis on the 11th post-injury day were made when the patient suddenly went into shock and died. The death was probably due to potassium intoxication as shown by the electrocardiogram. Autopsy revealed extensive burn changes in the right leg and left shoulder girdle. Microscopically, the kidney showed the changes of hemoglobinuric nephrosis.

Comment: From the second post-injury day until dialysis on the sixth post-injury day, the patient received 125 grams of sulfonate resin orally and 210 grams of sulfonate resin rectally (administered as 30 grams in 100 ml. of 10 per cent glucose in water.) During this time, the BUN rose from 75 mg. per cent to 242

per cent while the serum potassium fell from 6.2 meq./l. to 4.7 meq./l. The new sulfonate ion exchange resin appears useful in controlling the serum potassium level. This case demonstrates that with severe injury to tissue, there is a rapid rise of urea nitrogen and potassium in the blood. Dialysis was needed every two days to prevent death from uremic or potassium intoxication.

DISCUSSION

Contraindications to the Use of the Artificial Kidney

Hemodialysis is a relatively safe procedure in experienced hands. Children weighing as little as 20 pounds can be successfully dialyzed(3) using a polyvinyl catheter in the inferior vena cava as the source of the patient's blood. Since heparin is needed to keep the blood from clotting, severe bleeding may be a contraindication to dialysis. However, experience in Korea(4) by one of us (K.J.) using artificial kidney dialysis following severe abdominal wounds, has shown that this is usually of little consequence. Protamine sulfate counteracts any excess heparin effect on blood coagulation.

Indications for the Use of the Artificial Kidney

The artificial kidney is used to supplement good medical management. It is now being used earlier, with less hesitation, and is not a "last ditch" measure. The general management of renal shutdown has been adequately presented in other papers(3, 4, 5, 6) and will not be discussed here. In general, the artificial kidney should be used to:

1. Remove uremic poisons so as to negate their severe metabolic and symptomatic consequences, e.g., acidosis, hyponatremia, hyperphosphatemia, hypersulfatemia, stupor, asthenia, convulsions, hypoventilation, absent cough reflex and death.
2. Remove diffusible poisons, such as aspirin and barbiturates.
3. Prevent death from potassium intoxication following renal shutdown.

Kolff systematically lists the possible indications for treatment with the artificial kidney.(7) A modified list of indications is shown in Table 1. Dialysis by means of the artificial kidney may be useful in any of the five classifications in Table 1. In the first three classifications there is renal damage which decreases renal function. In these conditions, death often occurs because

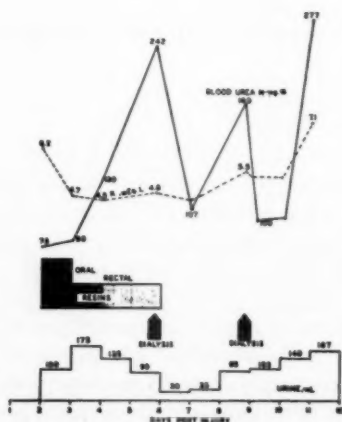


Fig. 7. Case 3. L.H. A 30 year old male with severe renal insufficiency following a severe electrical burn. Death probably due to potassium intoxication.

of renal insufficiency complicating the primary disorder. In many instances, the renal lesion can heal if given enough time. The artificial kidney, therefore, may be used to tide over a patient until his own kidneys can heal and perform their normal function.

In the fourth classification in Table 1, the artificial kidney is used to remove dangerous exogenous poisons.(8, 9) In cases of barbiturate poisoning, mortality rates are quite low with conservative treatment; however, the morbidity is high, recovery is often slow and uncertain. Artificial kidney dialysis can shorten the morbidity and hasten recovery. At times, it will be life saving. Berman(9) reports that in barbiturate poisoning, there is strong indication for dialysis if the barbiturate blood level is over 8 mg. per cent with phenobarbital poisoning or over 3.5 mg. per cent with Seconal, Amytal or Nembutal poisoning. As much as 9.33 grams or 37 per cent of an ingested dose of barbiturate has been removed by artificial kidney dialysis. Aspirin can be removed 20 times as fast with artificial kidney dialysis as compared with ordinary kidney excretion(10).

Other miscellaneous uses of the kidney are not as well defined as the first four indications in Table 1. Cases of acute glomerulonephritis with severe uremia have appeared to be benefited. The procedure in some instances appears to be life saving. The possible use of the artificial kidney in chronic renal disease is poorly defined. It is our belief at the present time that cases of chronic renal disease which became suddenly worse because of a superimposed, acute, reversible condition, such as sepsis or pulmonary infarction, can be helped by dialysis. Dialysis is not curative but will enable the patient to live and return to the status that was present before the superimposed complication. As Kolff(7) states, six hours of dialysis may be the equivalent of six weeks of difficult, frustrating medical management. Hemodialysis may be useful in preparing a patient with uremia for surgery. Use of the artificial kidney, while safe and effective, is a fairly large undertaking. Each time dialysis is necessary, it requires constant supervision by a trained team for four to eight hours. It is becoming a procedure used much earlier in the course of conditions requiring its use. When proper indications exist, it is unwise to delay the procedure until the situation becomes critical or beyond repair.

INDICATIONS FOR TREATMENT WITH THE ARTIFICIAL KIDNEY

1. Acute tubular necrosis following hypotension due to
trauma
blood loss
bone fractures
carbon monoxide poisoning
2. Hemoglobin and myohemoglobinuric nephrosis due to
transfusion reactions
burns
hemolytic anemia
sickle cell crisis
eclampsia
hemolysis following use of water in transurethral prostatectomy
3. Toxins
bichloride of mercury
alloxan
carbon tetrachloride
cresol
diethylene glycol (anti-freeze)
poisonous mushrooms
sulfonamides
chlorate ion
bichromate
tartrate
roentgen contrast media (angiocardiology)
bacterial toxins
4. Intoxications without primary renal damage
bromides
acetylsalicylic acid
barbiturates
thiocyanate
5. Miscellaneous
acute glomerulonephritis
chronic renal disease
intractable edema
overwhelming diabetic acidosis

SUMMARY

Because of the availability in Arizona of a trained team utilizing the artificial kidney in cases of acute renal insufficiency or poisoning, the indications, contraindications and possible uses of artificial kidney dialysis are presented. Three cases of acute renal insufficiency treated with the artificial kidney are presented which demonstrate many aspects attendant on this problem. Artificial kidney dialysis is a new, safe weapon that can be used in the salvage of some patients with renal insufficiency or poisoning.

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THE GEOGRAPHIC DISTRIBUTION OF COCCIDIOIDES IMMITIS AND POSSIBLE ECOLOGIC IMPLICATIONS*

Keith T. Maddy, D.V.M., M.P.H.

INTRODUCTION

A NUMBER of interesting studies have shown how the ecological requirements of various micro-organisms affect the geographic distribution of certain infections in man and animals.

Aitken(1) pointed out the relationship of soil types in Iowa to the distribution of swine erysipelas indicating that only where the soil was slightly alkaline in reaction was *Erysipelothrix rhusiopathiae* likely to become established in the soil. Van Ness and Stein's study(2) indicated that the soils of the United States that were neutral or slightly alkaline, rich in nitrogen, moist and poorly drained were the ones in which *Bacillus anthracis* was most likely to become established.

Zeidberg(3) has offered data to show a correlation between a significantly higher number of histoplasmin-reacting persons and the presence of red-yellow podzolic soils in the locale. Zeidburg and Ajello(4) point out the correlation of large numbers of positive soil isolates of *Histoplasma capsulatum* and collections of soil specimens from environments exposed to chickens. Zeidberg, Ajello and Webster(5) report that soils from which *H. capsulatum* has been isolated had a higher acidity than negative soils. They point out that although in the laboratory *H. capsulatum* is capable of abundant growth over a wide range of pH, perhaps under natural conditions, the pH level is more important. Furcolow and Horr(6) have outlined the area of the United States where the average annual precipitation is from 35 to 50 inches and the average summer temperature is between 70 and 80 degrees F. The main part of this area is in the middle central and middle eastern states where a high level of histoplasmin sensitivity exists. They further point out that the direction of the prevailing winds over the area apparently tends to limit the spread of the fungus to eastern and northeastern United States. The area between the Appalachians and the Atlantic coastline is only mildly endemic although temperatures are within Furcolow's and Horr's selected ranges. This area is protected by mountains from the main endemic area. The prevailing winds of the

coastal area blow in a large circle over this area.

Plant pathologists have studied the relationship of climate to certain fungal infections in plants. Some of these studies have progressed to the point where epidemics of these infections can be predicted from weather observations.(7-17) Furcolow and Horr(6) show the significance of this in regard to histoplasmosis.

Smith(18) has shown where human infection with *Coccidioides immitis* have occurred in the United States. (See Fig. 1) Note the close similarity of this area with that known as Lower Sonoran Life Zone of the United States. (See Fig. 2)



Fig. 1. Endemic area of coccidioidomycosis in United States of America as designated by Smith in 1951.(18) (Reproduction permission granted by California Medicine.)



Fig. 2. Lower Sonoran Life Zone in the United States.

LOWER SONORAN LIFE ZONE

In 1898, Merriam(19) classified the United States into several biological life zones, one of which is the Lower Sonoran Life Zone. Since that time there have been numerous modifications and refinements of the life zone concept. These zones were first divided according to the sums of the degrees of temperature above a given temperature for a year, added to the mean temperature for the hottest six weeks. This classification was based on the knowledge that plants

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grow only when the environment is above a certain temperature. These zones were subdivided into their humid and arid provinces. The plant and animal life was studied as to its distribution within the zones. In broad geographic areas these life zones are useful in aiding general studies in plant and animal ecology. Hall and Grinnell (20) have pointed out that in small geographic subdivisions, studies in plant and animal association are found to be more useful in analyzing the ecology of the area. Slope exposure, air currents, streams carrying cold water, evaporation from moist soil, proximity to large bodies of water, influence of lingering snow banks and of glaciers, changes in vegetative covering, extent of a mountain area, rock surfaces, and other miscellaneous local influences can alter the life zone in a local area.

The Life Zone concept is empirical and as such, biologists do not agree on the number of zones to use or where to divide them. As an example, at the eastern end of the Lower Sonoran Life Zone, there is a question as to the exclusion from this zone of the Edwards Plateau in Texas and the exclusion of parts of northwest Texas and southwest Oklahoma. Biologists do not agree as to the value of the Life Zone concept in the study of plant and animal life; some prefer to use a Biotic Province concept for these studies.

The Lower Sonoran Life Zone is characterized by arid and semi-arid climates, with hot summers and few winter freezes, a low altitude, and an alkaline soil. This limits plants and animals to certain types that can survive in this environment. This environment, and only this environment, seems to permit *C. immitis* to exist in nature. Presumably the fungus grows primarily in the soil.

Possibly a careful study of the characteristics of the Lower Sonoran Life Zone, its possible subdivisions, and the plant and animal associations within the zone, in relation to areas of varying endemicity for coccidioidomycosis, would help in better understanding the epidemiology of this infection. Such a study is under way by the author in Arizona.

ARIZONA

This study began with the observation that the creosote bush, *Larrea tridentata* (See Fig. 3), grew in all those parts of the state where coccidioidomycosis was known to be endemic.

It was observed that the bush was not growing in any of the areas believed to be non-endemic. An opportunity presented itself to skin-test dairy cattle with coccidioidin in the Verde Valley. (The development and use of this test by the author in animals will be reported in a later paper.) This valley, which lies about 100 miles north of Phoenix, was believed to be out of the coccidioidomycosis area. Upon arriving in the valley, the author found creosote bushes growing in abundance and predicted that the area would be found to be an endemic one. Tests proved that a sizable per cent of the home-raised dairy cattle there were coccidioidin-positive. Although Bullhead City, Kingman, and Wikieup, in northwestern Arizona were out of the known endemic area, they are in the creosote bush locale (21,33,23) (See Figs. 4 and 5) and coccidi-



Fig. 3. The Creosote bush. (*Larrea tridentata*)



Fig. 4. Map of the Natural Vegetation of Arizona. (The dark areas of the Southwestern parts of the state are the creosote bush areas.) (Reproduction permission granted by University of Arizona.)

oidin tests on the cattle revealed infection. Fewer infections were found at the higher elevations. Just south of Kingman in the Hualpai Mountains a herd of cattle was tested. This was above the creosote bush terrain and in the Upper Sonoran Life Zone. No evidence of infection was found there in the home-raised animals. Some animals brought up there from Kingman, and from a known endemic area northeast of San Diego, California, were coccidioidin positive. About this time the author found that the creosote bush was used as one of the main indicator plants for designating the Lower Sonoran Life Zone, excepting some of the west Texas areas and the San Joaquin and Sacramento valleys of California which receive more rainfall and gradually blend into other life zones. The life zone maps are now found to be useful in predicting where endemic areas are likely to be present or absent; also altitude and rainfall, (24,25) and proximity to the edge of the Lower Sonoran Life Zone are considered in predicting approximate infectiveness of the area.

The map of the Lower Sonoran Life Zone in Arizona (Fig. 6) (26) shows that an endemic area could exist along the Colorado River across northern Arizona to the Utah line. Future projects will include some skin tests of persons and animals in these areas. A test on persons and animals on the Havasupai Indian Reservation down in the Grand Canyon would be an interesting test. A test on the mules that live in the Transition Life Zone at the south rim of the Grand Canyon and make the trip down to the floor of the canyon through the Upper Sonoran Life Zone and into the Lower Sonoran Life Zone with tourists would be of interest in checking the correlation of the life zone and endemic areas. The United States Bureau of Reclamation plans to build several dams on the Colorado River in northern Arizona; perhaps some of the employees will become infected in this area, which previously was considered to be well out of the endemic zone.

Studies on the Indian reservations of Arizona by Aronson, Saylor, and Parr (27) revealed a high percentage of skin-test positive persons on the Papago, Pima and San Carlos reservations. These reservations, which are located in south central Arizona, are at low altitudes. At Fort Apache, at a much higher elevation, almost no infection was detected by skin tests. Studies by the United States Army Air Corps, the Army Epi-

demiological Board, and the United States Air Force revealed that Luke Air Force Base near Phoenix, Williams Air Force Base near Chandler, Gila Bend Air Base near Gila Bend, and Marana and Davis Monthan Air Force Bases near Tucson were in quite endemic areas. (28,29) A World War II prisoner-of-war compound at Florence was found to be the most infective area known. Fifty per cent of the susceptibles in this compound were converted to a positive skin test within six months. (30)

Studies by Randolph and McMartin (31) and Emmett (32) on school children in the Phoenix

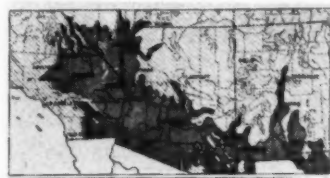


Fig. 5. Distribution map of the creosote bush (*Larrea tridentata*) over part of the southwestern deserts of the United States. (Reproduction permission granted by University of Arizona.)



Fig. 6. Map showing the Lower Sonoran Life Zone in Arizona. (Reproduction Permission granted by U. S. Department of Interior.)

area revealed a high rate of skin test positive individuals.

Observations of Prchal(33) and the author (34) on infections acquired by feedlot cattle have shown various areas of south central Arizona to be endemic. Skin tests are being made on a number of home-raised cattle throughout Arizona. Preliminary results show that in areas known to be infective for man there is also infectiveness for cattle. (These studies will be summarized in a later paper.) *C. immitis* is being found in new areas and the relative infectivity of the various areas is being determined.

Observations made during World War II, and more recent ones by Smith(35) reveal no endemicity at Fort Huachuca in the extreme southern part of the state. This fort is located above the Lower Sonoran Life Zone at about 5,000 feet altitude.

The extreme western, southeastern, and the northwestern parts of Arizona within the Lower Sonoran Life Zone apparently have low endemicity levels. Apparently the south central part of the state is the most infective area for mammals in the world known at present. In attempting to determine the factors that favor the natural propagation of the fungus, the author noted the following climatic characteristics in south central Arizona. The mean July temperature in the shade is around 90°F; the July mean maximum temperature is around 105°F. The mean January temperature is around 50°F; rarely does a freezing temperature occur at the ground level for more than a few hours. The rainfall averages about 9 inches per year; and falls mostly in two seasons—summer and winter. The mean relative humidity at 5:30 a.m. is about 59 per cent in July and about 82 per cent in January. The mean relative humidity at 5:30 p.m. is about 30 per cent in July and about 51 per cent in January. The soil is mildly alkaline in reaction. The vegetation is quite typical of the Lower Sonoran Life Zone but is somewhat more abundant than in other areas of the Zone as the rainfall is above average.

NEW MEXICO

A look at the Lower Sonoran Life Zone in New Mexico(36) (See Fig. 7) shows that infections could be expected to occur at places such as Lordsburg, Deming, Las Cruces, Hot Springs, Socorro, Alamogordo, Roswell and Carlsbad. It is noted that Santa Fe and Albuquerque are out of the Lower Sonoran Life Zone

and the creosote bush zone. Since Albuquerque is in the desert, some have expected to see coccidioidomycosis acquired there, but none has been diagnosed. The minimum winter temperatures in Santa Fe and Albuquerque are close to, or are possibly just below the minimum temperatures at which *C. immitis* can exist in nature.

TEXAS

In Texas the creosote bush belt(37) (Fig. 8) extends down along the Rio Grande, beginning at the south New Mexico line about 180 miles wide. This belt tapers as it follows the river southward and ends just south of Laredo. The most endemic areas in Texas are within this belt. The eastern extent of the Lower Sonoran Life Zone in Texas ends as the rainfall increases. Although most of eastern Texas and most of southeastern United States have just as many units of high temperature as the Lower Sonoran Life Zone, the rainfall is significantly higher; this area is called the Lower Austrial Life Zone. The Upper Austrial Life Zone just to the north is al-



Fig. 7. Map of the Life Zones of New Mexico. (The Lower Sonoran Life Zone is the grey area in the Lower half of the State.) (Reproduction permission granted by U. S. Department of Agriculture.)

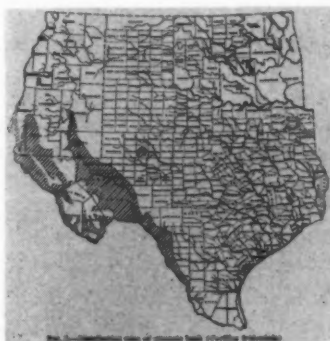


Fig. 8. Distribution area of creosote bush (*Larrea tridentata*) in Texas and parts of New Mexico. (Reproduction permission granted by U. S. Department of Agriculture.)

most identical with the endemic area for histoplasmosis. A number of indicator plant and animal species have been selected for the Lower Sonoran Life Zone in Texas. (37,38,39) (See Fig. 9) The eastern limit of the Lower Sonoran Life Zone is almost identical with the extent of the coccidioidomycosis endemic area as indicated by Smith. (18) The limiting factor to the flora and fauna at the eastern edge of the zone is the increased rainfall that permits other species of plants, fungi, and animals to thrive better, thus crowding them out.

UTAH

In Utah, the St. George area in the southwestern corner is known to be mildly endemic. Tests on school children by Myers, (40) and skin tests on cattle by Palmer, (41) reveal this area to be almost identical with that of the Lower Sonoran Life Zone. (See Fig. 10) Tests have not been made in the Lee's Ferry area. Although there are other arid areas further north, the two places mentioned are the only ones in Utah where the minimal winter temperatures stay high enough to permit flora and fauna of the Lower Sonoran Life Zone to exist.

NEVADA

In Nevada some human cases have been observed in the Las Vegas area. Skin tests by the author on dairy cattle revealed the Logandale-Overton area (60 miles north of Las Vegas) to be endemic. The Lower Sonoran Life Zone in Nevada (See Fig. 11) (42) is roughly below a line from St. George, Utah to Scottie's Castle in California's Death Valley. The Zone reaches north in the Nevada valleys almost to Caliente and Alamo, although the upper areas of the Mormon, Sheep and Charleston Mountains are out of the Zone. The arid area continues northward but minimum temperatures in the winter limit the flora and fauna typical of the Lower Sonoran Life Zone to the southern tip of the state.

CALIFORNIA

In California the entire Mohave and Sonoran deserts are within the Lower Sonoran Life Zone. (43) (See Fig. 12) Since relatively few people live in these desert areas, few studies have been possible. Not all of these two areas were included by Smith (18) in 1951 in the areas of proved endemicity. Willet and Weiss, (44) Pfanner, (45) Goldstein and McDonald, (46) and Plunkett, (47) and others have observed some human infections apparently acquired in the areas. The author (34) and other veterinarians have noted

that some feedlot cattle fed in the El Centro vicinity apparently get infected there. In any case, the entire Mohave and Sonoran deserts of California are likely to be only mildly or spottily endemic, an assumption which is based on the indicator flora. They receive the least rainfall of the entire Lower Sonoran Life Zone of the United States. This averages only about three inches per year, and sometimes this may fall all at one time; some years pass with no precipitation. As a result, vegetation is very sparse and soil fungi

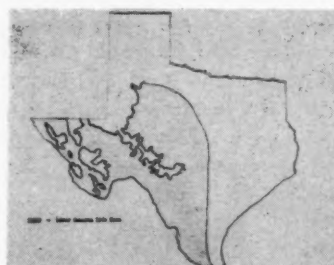


Fig. 9. Lower Sonoran Life Zone of Texas.

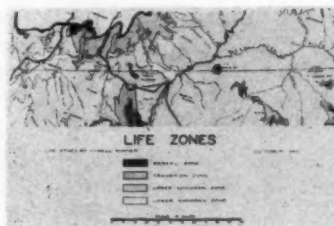


Fig. 10. Life Zones of the northern Arizona and southern Utah area. The Lower Sonoran Life Zone occurs in Utah in this area only. (Reproduction permission granted by the U. S. Department of Interior.)

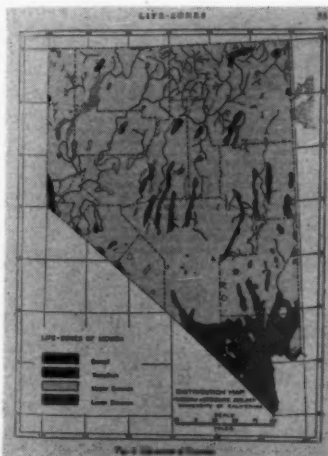


Fig. 11. Life Zones of Nevada. (The Lower Sonoran Life Zone is the dark area in the southern end of the state which is largely south of the 37th parallel.) (Reproduction permission granted by University of California Press.)

are relatively rare. (In this desert area, especially, termites serve as nature's main method of destroying dead vegetation.) Due to little rainfall to leach out the soil, the alkalinity of the area remains almost as high as when in geologic ages past much of it was under the sea. This high alkalinity is quite unfavorable to the growth of plants and fungi. This entire area has the almost-frost-free and arid climate apparently so favorable to *C. immitis*; but possibly the rainfall is too scarce and the soil too alkaline for abundant fungal growth, compared to the apparently more favorable areas of south central Arizona and the southern end of the San Joaquin Valley.

The areas near the coast in southern California, known to be endemic for man and animals, correlate very closely with the Lower Sonoran Life Zone. The main endemic area of the San Joaquin Valley fits almost exactly into the pattern of the Lower Sonoran Life Zone there. Here (as in Texas at the east end of the Life Zone) the creosote bush does not extend all the way to the edge of the Zone. Some other indicator plants and animals live there, as described by Hall and Grinnell.(20) It is interesting to see how both the Lower Sonoran Life Zone and endemic areas extend to a point just north of the highway between Tracy and Livermore. Endemic areas and the Zone correlate very well in the coastal valleys. The northern end of the Life Zone there begins just south of Salinas and extends down the valleys, including the towns of Paso Robles, Shandon and Simmler. Neither the known endemic area nor the Lower Sonoran Life Zone extends west to San Luis Obispo or Santa Barbara.

The Lower Sonoran Life Zone, as designated by Grinnell,(43) extends up the Sacramento Valley to Red Bluff. Smith(48) has noted several isolated human cases of coccidioidomycosis that apparently originated in Yolo County of this area. The author and some other veterinarians have noted the infection in a few feedlot cattle which apparently were infected in the Sacramento Valley. Although this area was designated as within the Lower Sonoran Life Zone and its soil may possibly support the growth of *C. immitis*, it is not nearly as suitable for the fungus as south central Arizona or the south part of the San Joaquin Valley. Throughout both the Sacramento and San Joaquin Valleys, the high temperature is relatively similar to the ideal area in Arizona. The heaviest endemicity in California

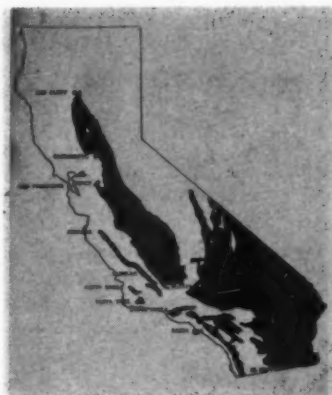


Fig. 12. Lower Sonoran Life Zone in California. (Black area.)

exists in the southern part of the San Joaquin Valley, with about 25 per cent of the susceptibles becoming infected per year.(29) As rainfall increases in the northern part of the San Joaquin Valley, the infection rates for coccidioidomycosis fall off. In the Sacramento Valley, the areas within the Lower Sonoran Life Zone receive more rainfall than the San Joaquin Valley to the south. It may be that the increase in rainfall to the north permits other competitive flora to crowd out *C. immitis*.

DISCUSSION

In ages past, the present southwestern desert areas of the United States had a humid climate. With the change to an arid and semi-arid area, only those organisms able to adapt to the new climate were able to survive. Aridity is said to serve as a stimulus to plant evolution.(49) Eventually specially adapted animals, plants and fungi likely evolved. (Emmons and Ashburn(50) have speculated that *Haplosporangium parvum*, a fungus found in various parts of the United States and Canada, may have mutated under desert conditions to produce *C. immitis*.) Biologists refer to the migration of some of the species of plants and animals from the main part of the southwestern deserts (Mohave and Sonoran) east over the Continental Divide into the Chihuahuan Desert in southern New Mexico and into western Texas. Migration of flora and fauna from the main southwestern desert area into the San Joaquin Valley and into some of the coastal valleys of California is said to have occurred. Seeds and spores of plants and fungi are carried on the bodies and in the digestive tracts of animals that migrate into areas suitable for their existence and if conditions are favorable in the

new environment, these flora multiply.

Perhaps *C. immitis* originated in the area now known as central Arizona which seems most favorable for its existence. Through the centuries it possibly has migrated to all favorable environments in the southwest. Within the next several thousand years, with some adaptive changes, it may migrate farther east in Texas and farther north in California. In any case, the spread of the endemic area should concern man very little considering the many years that likely are necessary for such expansion.

Studies on plague in the United States at one time centered around the San Francisco area where human cases were discovered. Further studies revealed that wild rodents in the area were infected. Studies were then extended beyond San Francisco over the entire western United States. Thus to some observers, the infection appeared to be spreading from a focus at the San Francisco port. If the wild animal studies had been started in western Colorado and had been extended to the Pacific, it would have appeared that the disease was spreading in the opposite direction. Possibly plague has existed in western United States long before the advent of man.

Psittacosis presented a parallel. Human cases associated with birds imported through the San Francisco port were observed. Further studies revealed infections in domestic fowl and wild birds in the San Francisco area. To some this appeared to be an imported disease. Possibly this virus had been around for a long time.

The same is true with coccidioidomycosis. Most of the early studies dealt with the San Joaquin Valley. Many medically-trained persons think of this infection when the valley is mentioned. As other areas are found to be endemic, the thought that comes to mind is that the fungus has migrated to these "new" areas. But what is "new" to man is not necessarily "new" in nature.

The endemic area of coccidioidomycosis extends down into the desert areas of Mexico. (51) There are endemic areas in Paraguay, (52) Argentina, (53) and Venezuela. (54) It is even remotely possible that the fungus was originally brought to our deserts from these other areas in dust on the bodies of migratory birds. One of the main indicator plants, the creosote bush, also exists in the desert areas of South America. (It is in the same genus, but some botanists say it is a different species.) It would be of interest to

check other desert areas of the world for flora indicative of the Lower Sonoran Life Zone.

The work of Emmons (55) indicated that possibly some of the desert-living rodents get severe disseminated infections. It has been suggested that these animals may play a role in the maintenance of the fungus in nature. Many species of these small mammals live entirely within the Lower Sonoran Life Zone.

Egeberg (56) has suggested the following to be favorable for a coccidioidomycosis endemic area: very hot summer months, mild winter weather, a period of precipitation, a soil with sparse vegetation which results in much dust, and winds.

Egeberg and Ely (57) report that in a soil-sampling survey for *C. immitis* in an area of the southern San Joaquin Valley of California, more soil specimens were found positive at the end of the rainy season than at the end of the dry season. Soil specimens taken in or near rodent holes, especially at the end of the wet season, were more likely to be positive than samples taken from soil sites at random.

Lubarsky and Plunkett (58) report that *C. immitis* grows better in sterilized soil than in non-sterilized soil, and that it grows on sand as well as on dead vegetation. In the laboratory they demonstrated that soils from various places in the United States supported the growth of *C. immitis*, and that temperatures as high as 42° and as low as -20°C. did not destroy the fungus as long as it was already growing in a soil sample. They also found that the fungus grows over all the pH ranges found in most soils.

Plunkett (47) has pointed out, however, that although the ideal conditions for maximum growth and sporulation of *C. immitis* can be determined in the laboratory, the true ecology of this fungus can be learned only by studying the organism in its natural habitat.

Freidman, Smith, Pappagianis, and Berman (59) studied the effects of various temperatures, humidities and amounts of salt in the media on one strain of *C. immitis*. Dry spores were stored at temperatures from -15°C. to 37°C. with relative humidities from 10 to 95 per cent. There was little loss in viability at any of the temperatures less than 37°C, until the sixth month at which time the count decreased not more than 50 per cent of the initial count. Ten per cent humidity and 37°C. was deleterious, but all the spores were not killed until six months had

passed. At 50°C. all the spores were dead in two weeks. Long storage of dry spores followed by subjection to extremes of temperature resulted in little loss of viability unless followed by a second storage period. Storage of spores in physiologic saline solution for similar temperatures and time periods resulted in more rapid loss of viability under extremes of temperature; at 4°C. the spores were just as viable six months later. Spores suspended in distilled water at 4°C. remained viable for 11 months. In saturated sodium chloride solution at 4°C. there was little loss of viability but at 37°C. the rate of death was more rapid. These studies indicate that *C. immitis* has adaptations that help it to survive in its arid habitat.

Although still too preliminary to summarize in detail, studies and observations by the author have indicated a number of ecological factors regarding the growth and propagation of *C. immitis*. In addition to man, many mammals in the endemic areas eventually become infected. Most of these mammals likely get infected from the soil, the common source of the fungus. In most of these mammals the fungus reaches a dead end.

Apparently the dog develops disseminated infections more often than man. In a study of over 100 cases of naturally-acquired disseminated coccidioidomycosis in dogs, the author found that some of the severely infected ones had sputum and urine with high spherule counts. Some had draining lesions on the body surface; with exudates with high spherule counts. When such exudate or urine is streaked on Sabouraud's media, the mycelia grows out in 48 hours. In one group of 10 dogs with disseminated infections, smears were made from a fresh fecal specimen from each dog. These were cultured on four tubes of fortified Littman's ox-gall media per dog. *C. immitis* was isolated (proved by mouse inoculation procedure) from four of these tubes, each from a different dog. Stools from these 10 dogs were placed on the shady side of a building for two weeks. All suspicious fungi that grew on the stools during the two week period were checked. Two specimens from two of the dogs, from which direct smears had revealed the fungus, were proved by mouse inoculation, to have the mycelial form of *C. immitis* growing on the stools. Previous to this study, soil samples from this immediate area were negative for *C. immitis*. Although infected animals possibly do contaminate their environment, it is likely that they

play a very minor role in the over-all epidemiology of coccidioidomycosis.

C. immitis in spherule form in pus from a granuloma about to break through the skin of an infected dog was placed on fortified Littman's ox-gall tubed media and immediately placed at -10°C. It remained viable for three months, about 25 per cent of the time. At 5°C. for three months it remained viable about 75 per cent of the time, at 35°C. for three months almost 100 per cent of the time, and at 45°C. for three months 0 per cent of the time. Further studies are planned using soil as a growth medium.

Soil sampling studies under way by the author in co-operation with the Arizona State Department of Health indicate that *C. immitis* is rarely isolated from irrigated, cultivated soil in the endemic area. So far, it appears that *C. immitis* can be isolated with some certainty only from in and around rodent holes in the desert.

It appears that *C. immitis* can grow only where there is a definite period of very hot weather during which there is little or no rainfall. During this period of time the surface soil becomes somewhat sterilized. *C. immitis* likely remains viable just below the sterile layer of soil, as well as in the moister and more nitrogen-rich environment of desert rodent holes. When a rain does eventually fall, the humidity in the surface soil probably approaches the optimum for the growth of the fungus. *C. immitis* grows well until other soil micro-organisms interfere with its growth or until the soil dries. The fungus probably still grows for a while down in the earth cracks and holes until the humidity in these sites drops and/or other soil micro-organisms interfere with its growth. At this time the environment is the most infective with winds picking up dust and arthrospores and carrying them about. A study of prevailing winds over the entire endemic area does not give any over-all clue to spread of this fungus, as was suggested for histoplasmosis by Furcolow and Horr.(6) Possibly the fungus cannot remain viable for long periods of time when airborne. A majority of human and animal infections seem to occur during the windy, dusty weather following the wet season. The sun again begins sterilizing the surface soil and the infection rates begin to drop. Infections can still occur in the season between peaks of infectivity. These are sometimes associated with digging in the soil and thus exposing viable spores. Infections are often seen in dogs

that dig in rodent holes while hunting on the desert, or are taken into new home sub-divisions where the soil has been graded. People too sometimes become infected in these new developments. An outbreak in a sizeable group of airmen who dug a ditch across an airbase near Tucson, (60) Arizona, and an outbreak in students who excavated for a building foundation near Bylas, Arizona, (61) are examples, as well as others such as the one of a group of students digging out a snake described by Davis, Smith and Smith, (62)

A study of various subclimates within the Lower Sonoran Life Zone is of interest. As an example, the following three areas may be compared climatically: 1. St. George, Utah which is just within the northern limit of the Lower Sonoran Life Zone in Utah and which is mildly endemic for coccidioidomycosis and is also about the northern limit for the endemic area in that part of the country; 2. Florence, Arizona which is apparently the most endemic area presently known for coccidioidomycosis; and 3. Yuma, Arizona, a hot and quite arid area which is apparently only mildly endemic for coccidioidomycosis (See Table I.) Study of data of this type will no doubt elucidate the factors in nature that affect the growth of *C. immitis*. It appears that the coldest area that will support this fungus has a mean minimum January temperature of about 25.0°F. Arid and semi-arid areas warmer than this likely can support the natural growth of this fungus. Although the temperatures at Yuma and Florence are quite similar, there is considerably more rainfall at Florence. Gila Bend, about halfway between these two places, has a mean annual rainfall of 5½ inches. Gila Bend's tempera-

tures are very similar to those of Florence and Yuma. The Gila Bend area is somewhat endemic for coccidioidomycosis. Perhaps about five inches per year in these high temperature areas is just about enough to create a substantially endemic area. In the hot weather areas with five inches to 20 inches of rainfall, it appears that the best conditions for the growth of this fungus are produced.

The exact rainfall as usually measured is apparently not as important as the precipitation effectiveness which is determined by run-off, evaporation, temperature, vapor pressure and other factors such as the season at which the rainfall occurs. The suitable moistening of the topsoil at the time of the year or season when the temperatures are most ideal result in the development of the most desirable humidities in the top-soil, that are optimum for certain plants, fungi and bacteria. (68)

The exact measured rainfall in the three heavily endemic areas in the United States is different, but the effective precipitation appears to be much less different. (68, 24) The soil type in the area has a good deal to do with water-holding capacity. The soil group that is almost synonymous with the Lower Sonoran Life Zone is designated as the "Reddish soils of the semi-arid to arid Southwest." This group is made up of Red Desert, Reddish-Brown, and Non-calcic Brown soils with much Lithosol. (69) In local areas the soil can vary considerably in type and consistency and consequently in the amount of rainfall necessary to maintain a given amount of moisture in the topsoil for a given period of time.

The three heavily endemic areas for coc-

TABLE I

Selected Climatic Data for U. S. Dept. of Commerce Weather Bureau Stations of St. George, Utah; Florence, Arizona; and Yuma, Arizona for the period of 1931 through 1952. (63,64,65,66,67) (All temperatures are given in Fahrenheit.)

Climatic Factors	St. George Utah	Florence Ariz.	Yuma Ariz.
Mean maximum temperature for July	101.4	106.6	105.5
Mean temperature for July	83.4	90.3	89.3
Mean maximum temperature-annual	77.4	87.3	87.0
Mean temperature-annual	60.8	69.8	69.3
Mean maximum temperature for January	52.5	66.0	67.1
Mean minimum temperature-annual	44.1	52.3	52.5
Mean temperature for January	38.9	50.7	51.0
Mean minimum temperature for January	25.3	35.4	35.0
Mean relative humidity-5:30 A.M. July	61%*	59%*	57%
Mean relative humidity-5:30 P.M. July	44%	30%*	32%
Mean relative humidity-5:30 A.M. January	82%*	83%*	71%
Mean relative humidity-5:30 P.M. January	68%*	52%*	48%
Annual rainfall (inches)	8.84	9.73	3.32
Mean number of days above 32°F. annual	210	345	362
Altitude in feet above mean sea level	2880	1498	199

coccidioidomycosis in the southwest as indicated by Edwards and Palmer's(70) skin-test study include Kern County, California, Pima, Pinal, and Maricopa counties in Arizona as well as the counties in Texas starting at the southeast corner of New Mexico and running southeast to below Laredo. A study of data from representative weather stations in these areas is of interest. (See Table 2.)

More than about 25 inches of rainfall per year in a hot climate appears to be undesirable for propagation of this fungus.

No doubt, further studies will shed more light on those ecological factors which determine the growth, propagation and dissemination of *C. immitis* in nature.

SUMMARY

A close correlation has been observed between the geographic areas of the Lower Sonoran Life Zone and the known endemic areas for coccidioidomycosis in the United States. There are indications that only within this life zone can *Coccidioides immitis* propagate in nature. A preliminary study reveals this likely reflects the need of the fungus for an arid or semi-arid climate, an alkaline soil, relative freedom from severe frosts, and a very hot dry season of several months followed by some rain. July mean temperatures from 80°F. to about 90°F., January mean temperatures from 39°F. to about 53°F., and an annual rainfall of about 5 to 20 inches seems to be the most ideal for the propagation of the fungus in nature. The parts of the Lower Sonoran Life Zone with a more arid or less arid climate, or with lower summer

mean temperatures are apparently less favorable areas for the fungus to propagate.

Some areas of the Lower Sonoran Life Zone that had not been delineated as endemic zones for coccidioidomycosis are now so designated by the author who coccidioidin-tested cattle raised in these areas. Other areas where *Coccidioides immitis* infections could be expected to occur have also been designated.

ACKNOWLEDGEMENTS

The writer expresses appreciation to the following for their review and helpful criticisms: C. E. Smith, Dean of the School of Public Health, University of California, Berkely; J. McCleary, Professor of Botany, Department of Biological Sciences, Arizona State College, Tempe; H. G. Crecelius, Arizona State Department of Health, Phoenix, Arizona; L. Jurwitz, U. S. Department of Commerce, Weather Bureau, Phoenix, Arizona and M. L. Furcolow and L. Ajello of the Communicable Disease Center.

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TABLE 2
Climate Summary For Weather Stations at Bakersfield, California,
Florence, Arizona and Del Rio, Texas 71

COUNTY AND STATE	STATION	TEMPERATURE					KILLING FROST AVERAGE DATES			AVERAGE PRECIPITATION																
		LENGTH OF RECORD	JANUARY AVERAGE		JULY AVERAGE		MAXIMUM	MINIMUM	LENGTH OF RECORD	LAST IN SPRING	LAST IN FALL	DROPPING SEASON	LENGTH OF RECORD	JANUARY	FEBRUARY	MARCH	APRIL	MAY	JUNE	JULY	AUGUST	SEPTEMBER	OCTOBER	NOVEMBER	DECEMBER	ANNUAL
			YR.	% P.	% S.E.	% F.	% F.																			
KERN		YR.	% P.	% S.E.	% F.	% F.	YR.				DAYS	YR.	IN.	IN.	IN.	IN.	IN.	IN.	IN.	IN.	IN.	IN.	IN.	IN.	IN.	
CALIFORNIA	BAKERSFIELD	36	47.0	83.5	118	13	36	FEB. 21	NOV. 25	277	40	1.06	1.06	1.06	.56	.42	.07	.01	.01	.11	.33	.54	.84	6.12		
PINAL																										
ARIZONA	FLORENCE	22	50.6	90.0	117	11	24	MAR. 12	NOV. 17	250	25	1.06	.91	1.00	.40	.18	.16	1.42	1.58	.87	.36	.85	1.48	10.31		
VAL VERDE																										
TEXAS	DEL RIO	33	52.3	86.5	111	12	33	FEB. 22	NOV. 28	280	33	.54	.71	.65	1.48	2.42	2.29	2.11	1.35	.347	.219	.117	.02	16.48		

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VIOFORM®-HYDROCORTISONE CREAM: A CLINICAL REPORT

By Kenneth C. Baker, M.D.

Tucson, Arizona

THE PURPOSE of this report is to relate the results of a clinical evaluation of Vioform®-Hydrocortisone Cream* in a group of 155 patients with various dermatological disorders. The preparation used in this study contained Vioform (idiochlorhydroxyquin, U.S.P., CIBA) three per cent and hydrocortisone (as the free alcohol) U.S.P., one per cent in a water washable base with a pH of about 6.5.

Vioform, a derivative of chlorhydroxyquinoline containing 41 per cent iodine, has been utilized for over 50 years to treat many diseases of man. It has gained wide acceptance and use as a therapeutic agent in the practice of dermatology because of its effectiveness, the low incidence of irritation and sensitization associated with its topical use, its antibacterial and antifungal properties, and its compatibility with many drugs commonly used in treating disorders of the skin.(4, 5, 7, 9)

Hydrocortisone applied topically was first reported of value in selected dermatoses by Sulzberger and Witten in 1952,(10) and this initial report was soon followed by further observations in a larger series of patients(11). It has been shown that hydrocortisone has marked anti-inflammatory and anti-pruritic effects at the tissue level, the onset of action is rapid, the free alcohol is often more effective than the acetate, and undesirable, systemic, steroid effects have not been observed with judicious topical use.(6, 8, 12, 13)

Vioform-Hydrocortisone — Many individuals in different areas undoubtedly used locally prepared Vioform and hydrocortisone preparations in dermatologic therapy prior to the commercial introduction of the presently available Vioform-Hydrocortisone Cream. Allison first reported on the use of the combination in the treatment of seborrheic dermatitis in 1954.(1) Later the same year, Arnold reported the combination to be effective in circumscribed neurodermatitis and stated the combination seemed superior in many

conditions to either of the constituents used alone.(3) In a subsequent publication, Allison stated that Vioform and hydrocortisone had proved valuable in various dermatoses, particularly in seborrheic dermatitis, neurodermatitis, and a variety of hand eruptions.(2)

Results of Study — The following table presents the results of treatment with Vioform-Hydrocortisone Cream in a group of 155 patients.

Comments — Vioform-Hydrocortisone Cream was used as an adjunct, in most cases, to x-ray and grenz-ray therapy along with hypoallergic soap and cosmetics. The most dramatic results were observed in seborrheic dermatitis, chronic eczematous otitis (external) and intertrigo with eczematous dermatitis. Sycosis vulgaris, impetiginized dermatitis, perleche, and stasis eczema also responded very well, the only objection being the discoloration on some patients with prolonged use.

The preparation was notably free of primary irritation and only three patients showed sensitivity of varying degree. One patient with perleche developed sensitivity to Vioform; one patient with intertrigo and eczematous dermatitis (with associated severe sunburn) had a flare-up due to questionable sensitivity and gave a slightly positive response to patch testing with Vioform; and one case of sycosis vulgaris developed apparent sensitivity although the patch test to Vioform was negative. It should be pointed out that the incidence of sensitivity reactions to Vioform-Hydrocortisone Cream was low, though it can be anticipated in a small percentage of cases with any topical application.

Summary and Conclusions — Vioform-Hydrocortisone Cream, used in conjunction with a good dermatologic regimen, was a valuable adjunct in the treatment of a group of 155 patients with a variety of skin disorders.

Its topical application produced most dramatic results in seborrheic dermatitis, chronic eczematous otitis (external), and intertrigo with ezema-

*Material for this study was supplied by CIBA Pharmaceutical Products Inc., Summit, New Jersey.

tous dermatitis. Sycosis vulgaris, impetiginized dermatitis, perleche, and stasis eczema also responded well.

Since this paper was written, I have treated more than 137 patients with the cream and lotion with good to excellent results — 61 of

the patients received the preparations along with no other modalities. In the majority of these cases the response was very satisfactory. Four patients developed a local sensitivity and only 14 received no benefit or showed little or no response.

DIAGNOSIS	NO. OF CASES	RESULTS
Anogenital Pruitis	12	Good
Atopic Dermatitis	5	Fair to Good
Chronic Eczematous Otitis (External).....	19	Excellent
Contact Dermatitis	7	Fair to Good
Impetiginized Eczema	9	Good
Intertrigo with Eczematous Dermatitis	15	Good to Excellent
Lichen Simplex Chronicus	3	Good
Neurodermatitis	6	Good
Nummular Eczema	14	Good
Perleche	8	Good to Excellent
Seborrheic Dermatitis	29	Excellent
Stasis Eczema	14	Good to Excellent
Sycosis Vulgaris	8	Good to Excellent
Varicose and Idolent Ulcers	6	Good
TOTAL	155	

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NOT ALL INSECTS ARE HARMFUL

By Dr. J. N. Roney, Extension Entomologist

Agricultural Extension Service, University of Arizona

IN THIS wide, wide world, there are over one million identified insects, and possibly that many more unidentified.

Among those in the identified group are insects that attack crops — sometimes the foliage, the fruit, the flowers, the roots or the stems. Others feed on stored grain, household belongings, or food. Some feed on livestock, others on human beings.

So you see, wherever we go, or whatever we grow, there are insects. True insects have six legs — no more — no less.

If I should hold a balance-type scale in my hands, I could say that I have all the beneficial insects in one pan and harmful ones in the other. We know that if we destroy all of the beneficial insects, the harmful ones might destroy man.

Incidentally, it is estimated that there are more insects in one square mile of earth's surface than there are of all other forms of animal life in the world.

There are two types of beneficial insects — parasites and predators. Parasites deposit their eggs in or on the harmful insects and the larvae or maggot that hatches kills the insect when it feeds. Predators feed upon the insect and destroy it before our very eyes.

Some insects which are harmful to man are beneficial to crops since they pollinate our flowers, or fruit trees, or other plants.

Now, let's see just what some of these beneficial insects are and how they benefit mankind. Quite often we will find heavy infestations of plant lice, or aphids, on flowers, or cabbage, cauliflower, radishes, etc. These small, soft-bodied insects suck the juice out of plants and may possibly kill the plants.

Sometimes when we find our plants covered with aphids, we also find a host of small, red insects with black spots on their wings. These are the common convergent ladybug. This ladybug feeds on the aphids and may clean up an infestation. The adult ladybug deposits small,

yellow, oblong eggs in a mass of from 15 to 20. From these eggs hatch small larvae resembling a Gila monster. These larvae also feed upon the aphid.

There is also a very small wasp that deposits its eggs in aphids and as the eggs hatch, the larvae eats out the inside of the aphid, thus killing it. Several days later when the larvae is grown, it cuts a hole in the back of the aphid and emerges. The dead aphid by this time is a straw color.

The lacewing fly is a small, green insect with wings shaped like a tennis racket. It has golden eyes. This fly lays its oval-shaped egg on a little hair and from that hatches the aphid lion. It is shaped somewhat like a carrot with little clippers in front. It feeds on many aphids as well as on other insects.

There are many ground beetles which feed on both soil and plant insects, in both the adult and larval stage.

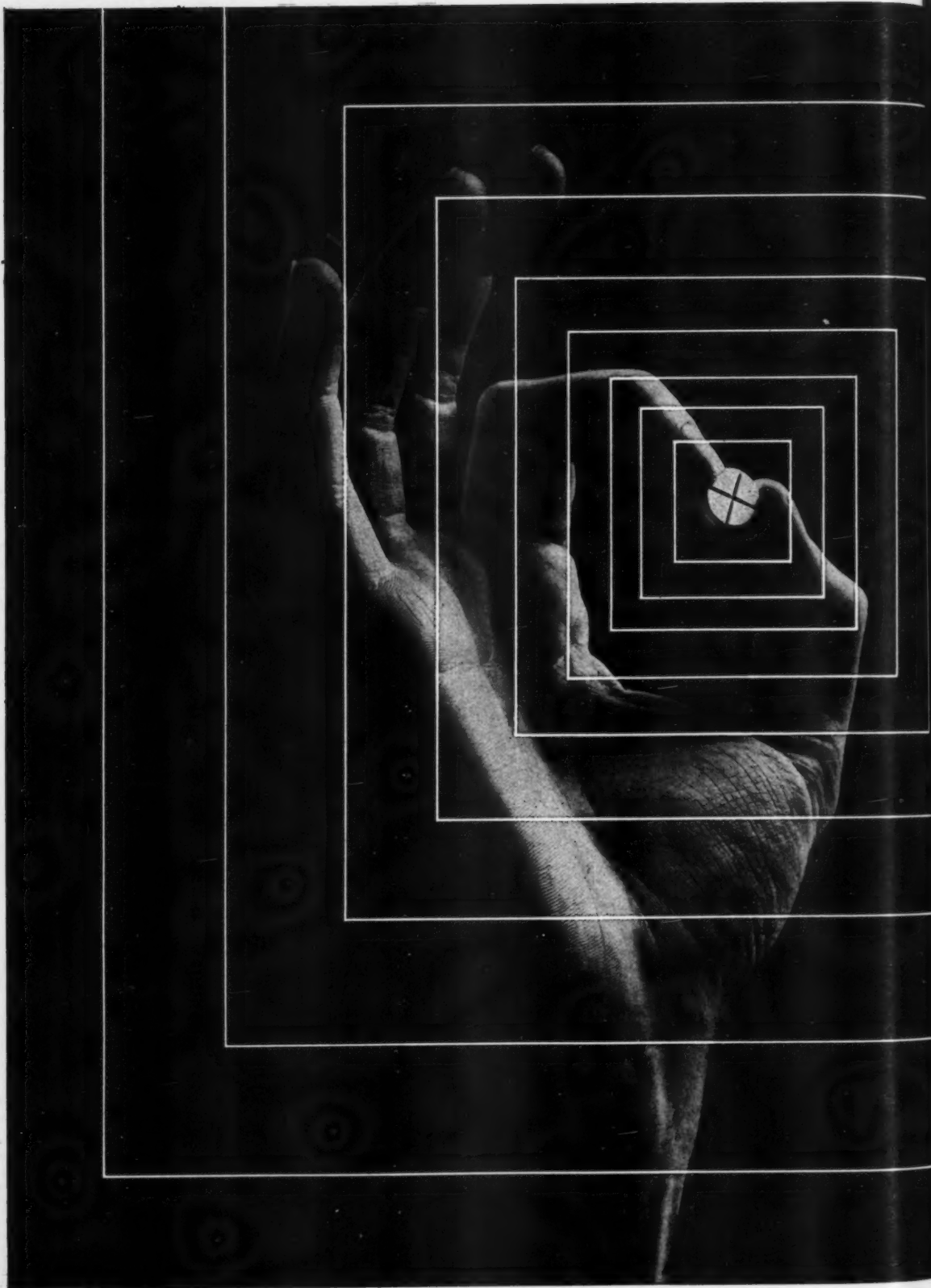
The praying mantis is also very beneficial since it feeds wholly on other insects.

There are also many small beetles, (true bugs) having only a hair-like beak for mouth parts, as well as certain wasps and flies that kill worms and adults of certain insects. Some in the true bug group are the big-eyed bug, the minute pirate bug, certain stink bugs, and assassin or kissing bugs.

If we find cottony cushion scale on pittosporum, we will not, as a rule, use an insecticide. Instead, some Vedalia, or Australian lady bird, beetles are planted in the infested shrub.

This particular ladybug was found in Australia about 1880 and was brought to California. It was released in infested citrus groves and today still economically controls the cottony cushion scale so often found in citrus.

So you see, not all insects are harmful, and when trying to control those that do damage, we must be careful not to eradicate those that do good or the balance could be upset.



a new era

in sulfa therapy

ONLY ONE TABLET A DAY

KYNEX*

SULFAMETHOXYPYRIDAZINE (3-SULFANILAMIDO-6-METHOXYPYRIDAZINE) **LEDERLE**

New authoritative studies prove that KYNEX dosage can be reduced even further than that recommended earlier.¹ Now, clinical evidence has established that a single (0.5 Gm.) tablet maintains therapeutic blood levels extending beyond 24 hours. Still more proof that KYNEX stands alone in sulfa performance—

- Lowest Oral Dose In Sulfa History—0.5 Gm. (1 tablet) daily in the usual patient for maintenance of therapeutic blood levels
- Higher Solubility—effective blood concentrations within an hour or two
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- Convenience—the low dose of 0.5 Gm. (1 tablet) per day offers optimum convenience and acceptance to patients

NEW DOSAGE. The recommended adult dose is 1 Gm. (2 tablets or 4 teaspoonfuls of syrup) the first day, followed by 0.5 Gm. (1 tablet or 2 teaspoonfuls of syrup) every day thereafter, or 1 Gm. every other day for mild to moderate infections. In severe infections where prompt, high blood levels are indicated, the initial dose should be 2 Gm. followed by 0.5 Gm. every 24 hours. Dosage in children, according to weight; i.e., a 40 lb. child should receive ¼ of the adult dosage. It is recommended that these dosages not be exceeded.

TABLETS: Each tablet contains 0.5 Gm. (7½ grains) of sulfamethoxypyridazine. Bottles of 24 and 100 tablets.

SYRUP: Each teaspoonful (5 cc.) of caramel-flavored syrup contains 250 mg. of sulfamethoxypyridazine. Bottle of 4 fl. oz.

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The President's Page



IT WAS A GREAT SOURCE OF PLEASURE TO ME AND TO EVERY DOCTOR TO WHOM I HAVE TALKED, THAT OF THE 10 OUTSTANDING YOUNG MEN PICKED BY THE NATIONAL JUNIOR CHAMBER OF COMMERCE, FIVE WERE DOCTORS OF MEDICINE. THESE AWARDS WERE GIVEN IN PHOENIX JAN. 18, 1958. WE HAVE A RIGHT TO BE PROUD OF OUR PROFESSION AND ITS YOUNG MEN COMING ALONG TO CONTINUE THE ADVANCES OF MEDICINE AND SCIENCE.

THE CANCER SEMINAR HELD IN TUCSON JAN. 23-25 WAS AGAIN AN OUTSTANDING MEETING. THE ATTENDANCE WAS GOOD. THOSE OF YOU WHO MISSED IT SHOULD PLAN ON ATTENDING NEXT YEAR.

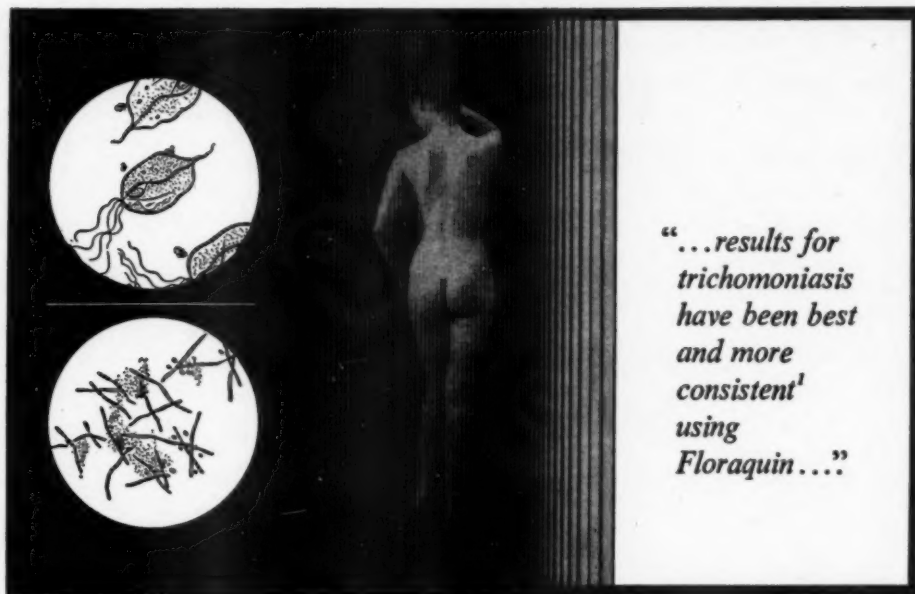
THE 67TH ANNUAL MEETING OF THE ARIZONA MEDICAL ASSOCIATION WILL BE HELD AT SAN MARCOS HOTEL APRIL 30, MAY 1, 2 AND 3. DOCTOR MANNING HAS AN EXCELLENT PROGRAM OUTLINED. AN INNOVATION THIS YEAR WILL BE TO CUT THE LECTURES AT 1 P.M. SECTIONAL MEETINGS WILL FOLLOW. FOR THOSE OF YOU WHO ARE SPORTS-MINDED THE FACILITIES OF SAN MARCOS GOLF COURSE WILL BE AVAILABLE EACH AFTERNOON. THIS WILL ENABLE ALL OF YOU TO WARM UP FOR THE TOURNAMENT SATURDAY, MAY 3. THIS SHOULD BE AN EXCELLENT MEETING. I URGE ALL OF YOU TO MARK YOUR CALENDAR NOW. PLAN ON BEING PRESENT FOR ALL THE MEETINGS.

C. C. CRAIG, President

Arizona Medical Association, Inc.



EFFECTIVE, DEPENDABLE THERAPY FOR VAGINITIS

An advertisement for Floraquin. It features a central illustration of a woman's back, seen from behind, standing in a dark, shadowed area. To the left of the woman are two circular insets. The top inset shows a microscopic view of trichomonads, which are pear-shaped organisms with flagella. The bottom inset shows a microscopic view of monilia, which are yeast-like organisms with long, branching hyphae. To the right of the woman, there is a quote in italics: "...results for trichomoniasis have been best and more consistent¹ using Floraquin..."

Floraquin® eliminates trichomonal and mycotic infection; restores normal vaginal acidity

Leukorrhea is by far the most frequent symptom of vaginitis; trichomonads and monilia are the most common causes. Many authors have reported² trichomonal protozoa in the vagina of 25 per cent of obstetric and gynecologic patients. Increased use of broad spectrum antibiotics has resulted in a sharp rise in the incidence of monilial infections.

Floraquin effectively eradicates both trichomonal and monilial vaginal infections through the action of its Diodoquin® content. Floraquin also furnishes boric acid and sugar to restore the normal vaginal acidity which inhibits patho-

gens and favors the growth of protective Döderlein bacilli.

Pitt¹ recommends vaginal insufflation of Floraquin powder daily for three to five days, followed by acid douches and the daily insertion of Floraquin vaginal tablets throughout one or two menstrual cycles. G. D. Searle & Co., Chicago 80, Illinois. Research in the Service of Medicine.

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SEARLE

Program

ARIZONA MEDICAL ASSOCIATION INC. ANNUAL MEETING APRIL 30—MAY 1, 2, & 3, 1958 CHANDLER, ARIZONA

WEDNESDAY—APRIL 30

- 10:00 Council Meeting
2:00 Blue Shield
6:30 Social Hour
Buffet

THURSDAY—MAY 1

- 8:00 House of Delegates
9:30 General Session Ceremonies
10:00-10:20 MacBryde
Modern Diagnosis and Treatment
of Hyperthyroidism
10:20-10:40 Pollack
Thyroid and Thyroid Cancer
10:40-11:00 Nolan
The Cytology and Treatment of
Carcinoma of the Cervix
11:00-11:15 Question and Answer Period
11:15-11:30 Intermission
11:30-11:50 Arrowsmith
Topic to be Announced
11:50-12:10 Del Regato
The Treatment of Carcinoma of
the Skin
12:10-12:30 Byars
Chronic Ulceration of the Skin
12:30-12:45 Question and Answer Period
1:00 Specialty Luncheons
2:30-4:00 Motion Pictures
Clinical Shock—47 min.
Fractures—33 min.
6:30 Social Hour

FRIDAY—MAY 2

- 9:00-9:20 Elkins
Surgical Management of Hydro-
cephalus
9:20-9:40 Byars
Treatment of Peripheral-Vascular
Abnormalities of Congenital Origin

- 9:40-10:00 Deamer
Some Problems Presented by Nor-
mal Puberty
10:00-10:20 MacBryde
Problems in Growth and Sex De-
velopment
10:20-10:40 Question and Answer Period
10:40-10:55 Intermission
10:55-11:15 Del Regato
The Role of Radiotherapy in the
Treatment of Cancer of the Breast
11:15-11:35 Pollack
Complications of Breast Surgery
11:35-11:50 Byars
Surgical Treatment of Cancer of
the Mouth
11:50-12:05 Question and Answer Period
12:30 Specialty Luncheons
1. Pediatrics and Allergy—Deamer
Further Luncheons to be An-
nounced
2:30-4:00 Motion Pictures
Management and Mismanagement
of Breech Presentation—19½ min.
The Doctor Defendant—30 min.
Cancer Society Film
(title to be announced)
7:45 Dinner Dance

SATURDAY—MAY 3

- 8:00 House of Delegates
10:00-10:20 Nolan
Carcinoma of the Corpus Uteri
10:00-10:20 Deamer
Respiratory Allergy and Environ-
mental Control
10:40-10:55 Question and Answer Period
10:55-11:10 Intermission
11:10-11:30 Griffith
The Theories Regarding the Pre-
vention and Management of Ather-
osclerosis
11:30-11:50 Arrowsmith
Topic to be Announced
11:50-12:10 Griffith
The Physician's Responsibility to
the Patient with Heart Disease
12:10-12:55 Question and Answer Period
1:30 Golf Tournament

FACULTY FOR ARIZONA MEDICAL ASSOCIATION MEETING CHANDLER—MAY 1958

Cyril MacBryde, M.D., 634 N. Grande Blvd., St. Louis 3, Missouri, Associate Professor of Medicine, Washington University, Director, Metabolism & Endocrine Clinics, St. Louis, Mo., Washington University.

James Nolan, M.D., 1407 S. Hope Street, Los Angeles 15, Calif., Gynecologist, Los Angeles Tumor Institute, Asst. Clin. Prof. of Ob-Gyn, University of Southern California.

William R. Arrowsmith, M.D., 3503 Prytania Street, New Orleans, La., Head of Department of Medicine, Ochsner Clinic, Associate Professor of Clinical Medicine, Tulane, University.

Louis Byars, M.D., 100 N. Euclid Avenue, St. Louis 8, Missouri, Plastic Surgeon, Assistant

Professor Clinical Surgery, Washington University, St. Louis, Mo.

William C. Deamer, M.D., University of California, San Francisco 22, California, Professor of Pediatrics University of California.

Juan Del Regato, M.D., Penrose Cancer Hospital, 2200 N. Cascade, Colorado Springs, Colo., Radiologist, Head of Penrose Cancer Hospital, Colorado Springs, Colorado.

George Griffith, M.D., 1200 N. State Street, Los Angeles 33, Calif., Professor of Medicine, University of Southern California.

Charles Elkins, M.D., 2409 East Adams, Tucson, Arizona, Neurosurgeon, Tucson, Arizona, Formerly Assistant Clin. Prof. Neuro-Surgery, Western Reserve University School of Medicine.

Robert S. Pollack, M.D., Suite 2210, 450 Butter St., San Francisco 8, California, Dept. of Surgery, Stanford University School of Medicine, San Francisco, Calif.

GUEST SPEAKERS

CURRICULUM VITAE

Dr. MacBryde received his A.B. at Washington University and his M.D. at Harvard. After internship and residency at Barnes Hospital in St. Louis he studied and did research abroad in Vienna and Berlin. He returned to St. Louis in 1933 and since then has practiced medicine and done teaching and research at Washington University School of Medicine and Barnes Hospital. He has been an active contributor to the literature on metabolic and endocrine subjects and serves on the editorial boards of several national medical journals.

His book "Signs and Symptoms," a textbook on pathological physiology and medical diagnosis, is widely used by medical schools, students and practicing physicians. The third edition has just been published (Lippincott, 1957). This book has also been published in London, England, and issued in Spanish translation (in Madrid) and in Italian (in Turino).

Mr. MacBryde is a member of Phi Beta Kappa and of Sigma Xi. He is a Diplomate of the American Board of Internal Medicine, and a Fellow of the American College of Physicians.

He has been active in the American Society for Clinical Investigation, the Central Society for Clinical Research, the Endocrine Society, and the American Diabetes Association.

MODERN DIAGNOSIS AND TREATMENT OF HYPERTHYROIDISM

Symptoms and physical signs are still the most valuable aids in diagnosis. Uses and pitfalls of the various laboratory aids will be analyzed: the BMR, the PBI of serum, and the RAI uptake.

Treatment today allows several choices and involves judgment and experience. When to advise anti-thyroid drugs, or radioiodine therapy or operation will be discussed.

PROBLEMS IN ADOLESCENT GROWTH AND SEX DEVELOPMENT

In the years from 12 to 20, profound mental and physical change occur; when aberrations appear, they deserve prompt recognition and attention. To perceive deviations, normal limits must be known. Standards and limits of normal will be presented for: statural growth; the adolescent growth spurt; body proportions; epiphyseal closure; primary and secondary sex



Cyril M. MacBryde, M.D.

CYRIL M. MacBRYDE,
A.B., M.D., F.A.C.P.,
St. Louis Mo.

Associate Professor of Clinical
Medicine,
Washington University
Director, Metabolism and
Endocrine Clinics,
Washington University

characters at various ages.

Differentiation of congenital,

endocrine, nutritional and other means of diagnosis and treatment will be described, with ment.



Robert S. Pollack, M.D.

ROBERT S. POLLACK, M.D.

San Francisco, California

Age, 41, graduate of Dartmouth College, '38, Cornell University School of Medicine, '42, Member the Department of Surgery and Teaching Staff at Stanford University School of Medicine and the University of California School of Medicine. Consulting Surgeon to the Veterans Administration Hospital, Oakland, California and the United States Naval Hospital, Oakland, California. Has contributed approximately 40 publications and articles to surgical journals. A recent book entitled "Tumor Surgery of the Head and Neck," published by Lea and Febiger of Philadelphia; and a second book entitled "Treatment of Tumors of the Breast" to be published during 1958.

THYROID AND THYROID CANCER

The wide differences in the clinical manifestations of cancer of the thyroid gland have created considerable divergence of opinion as to its true pathologic character, and confusion as to proper treatment. Presentation, therefore, of this subject includes discussion of incidence, pathologic classification, the site and nature of metastasis, diagnosis and use of radioactive iodine, the relationship of cancer to adenomas, and method of treatment. This will include more recent surgical and medical innovations, emphasizing the rationale for the procedures to be recommended.



James F. Nolan, M.D.

JAMES F. NOLAN, M.D.

Los Angeles, California

Age, 43. Graduate of the University of Missouri '35, and Washington University School of Medicine 1938. Trained in the Washington University group of hospitals, now Assistant Clinical Professor of Obstetrics and Gynecology at the University of California. Chief of Service, Gynecology-California Hospital, Los Angeles. Active in the Manhattan Engineering Project.

1. Cytology in the Treatment of Carcinoma of the Cervix. This is a study of the material available from Papanicolaou smears before, during and after radiation treatment. This is being carried out in order to evaluate the possibility of assessing a prognosis by the cytological means. More specifically, the prime interest is to determine when radiation failure may be diagnosed.

Carcinoma of the body of the

COMPLICATIONS OF BREAST SURGERY

This subject is best divided into the immediate and latent complications which follow radical breast surgery. Factors such as control of hemorrhage, infection and morbidity from anesthesia, wound healing and motion of the arm will be discussed under the immediate group. In the latent group complications such as lymphedema of the arm and lymphangiosarcoma, pregnancy, the problems of the opposite breast and the management of metastasis will be discussed.

uterus. This is an attempt to (technically operable — consti- gery with and without pre-oper-
evaluate the efficacy of pre- tutionally operable) lesions. A tive radium in an unselected
operative radiation in stage 1 comparison of the results of sur- series will be presented.



Charles W. Elkins, M.D.

CHARLES W. ELKINS, M.D.

Tucson, Arizona

Western Reserve University
School of Medicine, 1937. For-
merly Assistant Clinical Profes-
sor of Neurological Surgery,
Western Reserve University
School of Medicine.

SURGICAL MANAGEMENT OF HYDROCEPHALUS

Hydrocephalus may be classi-
fied as congenital or acquired.
Congenital hydrocephalus may
be communicating or obstruc-
tive, while acquired hydroceph-
alus is usually the result of ob-
struction to the cerebro-spinal
fluid pathways.

It is thought that congenital
communicating hydrocephalus
results from decreased absorp-
tion of cerebro-spinal fluid.
Numerous shunting procedures
have been devised to divert the
flow of this fluid into body cavi-
ties such as the peritoneum or
urinary tract. It is thought that
such procedures arrest the pro-
gress of hydrocephalus until nor-
mal absorptive processes func-
tion.

Ventriculo-jugular anastomosis
has proved effective in accom-
plishing hydrocephalic arrest.

Editorial Page

ARIZONA MEDICINE

Journal of
ARIZONA MEDICAL ASSOCIATION, INC.

VOL. 15 MARCH, 1958 NO. 3

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The Editor sincerely solicits contributions of scientific articles for publication in ARIZONA MEDICINE. All such contributions are greatly appreciated. All will be given equal consideration.

Certain general rules must be followed, however, and the Editor therefore respectfully submits the following suggestions to authors and contributors:

1. Follow the general rules of good English, especially with regard to construction, diction, spelling, and punctuation.

2. Be guided by the general rules of medical writing as followed by the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.

3. Be brief, even while being thorough and complete. Avoid unnecessary words. Try to limit the article to 1500 words.

4. Read and re-read the manuscript several times to correct it, especially for spelling and punctuation.

5. Manuscripts should be typewritten, double spaced, and the original and a carbon copy submitted.

6. Articles for publication should have been read before a controversial body, e.g., a hospital staff meeting, or a county medical society meeting.

7. Exclusive Publication—Articles are accepted for publication on condition that they are contributed solely to this Journal. Ordinarily contributors will be notified within 60 days if a manuscript is accepted for publication. Every effort will be made to return unused manuscripts.

8. Illustrations—Ordinarily publication of 2 or 3 illustrations accompanying an article will be paid for by Arizona Medicine. Any number beyond this will have to be paid for by the author.

9. Reprints—Reprints must be paid for by the author at established standard rates.

The Editor is always ready, willing, and happy to help in any way possible.

(The Opinions expressed in original contributions do not necessarily express the opinion of the Editorial Board.)

PR—?

THE CRITICAL spotlight is turned on the medical profession—it behooves us to be alert constantly for possible breaks in our public relations.

It is the practice of a few physicians, through their answering services, to refuse all calls relative to the refilling of prescriptions. A few others will allow the telephone operators to screen the calls for "important" medications, such as digitalis and narcotics. Some doctors will not accept any calls for refills, except during office hours. A check upon the age group of doctors who have such attitudes reveals that these were all young physicians with one exception.

A prescription and the medicament it procures represents an important link between the doctor and the patient's recovery. This is true, irrespective of the ingredients. To the patient, it is very important to his recovery. All such medications are essential for the patient, or the trusted doctor would not have wasted the patient's money, by requesting him to procure it, and take it.

It is too bad that a few patients will err in trying to get old prescriptions refilled for new illnesses. It is also annoying that some seem intentionally to wait until weekends to have their medical needs refilled. We teach our clients that we are on call 24 hours a day seven days a week—so why should this not also apply to essential medications?

One physician, who was particularly distressed by these "needless calls," cited an example of a patient who, on a Saturday evening, desired to have a simple cough syrup refilled. This doctor taught him a lesson and refused to refill through the answering service. The doctor failed to properly analyze the situation. Yes,—It was just a simple stock cough syrup—he did not recall that the patient had been taking it for a long time, hence it was effective; that the patient had never before failed to call during duty hours; that the patient had severe emphysema and asthma, and irrespective of the ingredients, if the patient believed it helped him, then it was helpful. The doctor did not visualize that had this patient coincidentally come down with pneumonia during the weekend, that the patient and his family

would have been certain that the lack of medication was the cause of the pneumonia. The latter happening could have easily paved the way to a good malpractice suit, which I personally would not like to defend before a jury.

If doctors have practices so large that they can not possibly tolerate telephone calls regarding prescription refills, then they have too many patients, and the doctors should cut their loads.

Refusing to service patients, after the doctors have entered a contractual relationship, is indeed wrong.

Yes, it is a poor policy, legally wrong, and very poor public relations for physicians to refuse to accept calls, any time, relative to patients' medications. Our medical societies should take steps to right this wrong.

L.B.S.

GUEST EDITORIAL FORAND BILL

J. R. Schenken, M. D.

|| R. 9467 WAS introduced into the last session of congress by Rep. Aime Forand (Dem. R. I.). It represents the second major extension of compulsory social security, an act which forms the foundation of the Welfare State, U.S.A. The first extension was HR 7225 which makes disabled persons past 50 years of age eligible for federal social security benefits.

The Forand bill provides for hospitalization and specified surgical benefits, if the surgical services are performed by a board-certified surgeon or a member of the College of Surgeons. (A nice built-in method of creating a schism in the medical profession.)

About 13 million Americans will be eligible for its benefits and it will be financed by all persons who are now on the social security rolls, with the employe and the employer each paying an additional 2 to 3 per cent tax. Thus, the total social security contribution will be about 9.5 per cent of the earned income subject to social security tax. It also provides an increase of this earned income subject to social security tax from \$4,200 to \$6,000 per year.

If this bill should become law, socialism in the United States will be assured because it is estimated that within 25 years, 30 million to 40 million Americans will be dependent upon the government for their health care and practically all persons will receive social security checks. The Marxian philosophy of individual dependence upon the central government will have been adopted through the democratic processes of a republic. *No wonder Khrushchev recently stated that war and revolution were no longer necessary to achieve the objective of communism.*

Organized medicine has much more at stake than the fear of professional regimentation under socialized medicine. Organized medicine must fear the ravages of all of the evils of socialism in a totalitarian state.

Danger Realized

The medical profession represents an informed group of professional persons who not only know that health care under a regimented system of government control soon deteriorates into an impersonal, unsympathetic trade-like service, but it also knows as a body of responsible citizens, that the passage of the Forand bill would mean the destruction of the last vestige of individual responsibility. By this I mean that our enormous inheritance tax places in the hands of the government the right to distribute a substantial part of our personal lifetime earnings to those in whom we have no personal interest or who do not deserve such a gratuity; our confiscatory income tax destroys any possibility of accumulating enough wealth which could be used as risk capital, the means by which this nation has developed the highest standard of living of any nation in the world; and now the proposed expanded social security act will soon make the government largely responsible for the health care of this nation, as well as the custodian of the "savings" program for all of its citizens, a program which, because of its compulsory nature, is based on the thesis that Americans are incapable of taking care of themselves.

What To Do?

Organized medicine has done poorly in the national political ring. It has won only one major national political battle, the defeat of the Wag-

ner-Murray-Dingell bill in 1948. It immediately broke training after that victory and has not won a bout since. The worst defeat was the acceptance of the principle that health, education, and welfare are close relatives and should be combined under one cabinet post. Oscar Ewing could not have done it better because all one needs to create a welfare state is control of education and health; Bismarck, Lloyd George, and Lenin all proved that.

We must revitalize the force which was mo-

bilized to defeat the Wagner-Murray-Dingell bill. We must join forces with enlightened groups such as the U.S. Chamber of Commerce and our numerous voluntary insurance carriers in the United States. We must tell the American people that they are selling their birthright for a mess of pottage. And, finally and most important of all, we must make an all-out effort to analyze the health needs of the aging in order to provide on a voluntary but individual basis for the deficiencies which are present.

AWARD TO ARIZONA MEDICINE

ARIZONA MEDICINE, the Journal of the Arizona Medical Association, was awarded first place for general excellence among the journals published in this state. The award was made by the Arizona Newspapers Association.

The plaque was awarded to John McMeekin, publisher of Arizona Medicine, by Mr. Hartline of the Butler Paper Company.

At the meeting of the Arizona Newspapers Association, Mr. McMeekin was elected vice president of the association.



John N. McMeekin (left), Publisher of Arizona Medicine is shown receiving the plaque for first prize in General Excellence at the annual contest of the Arizona Newspapers Association. Mr. Dave Hartline of the Butler Paper Co. presented the plaque.

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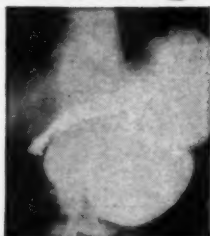
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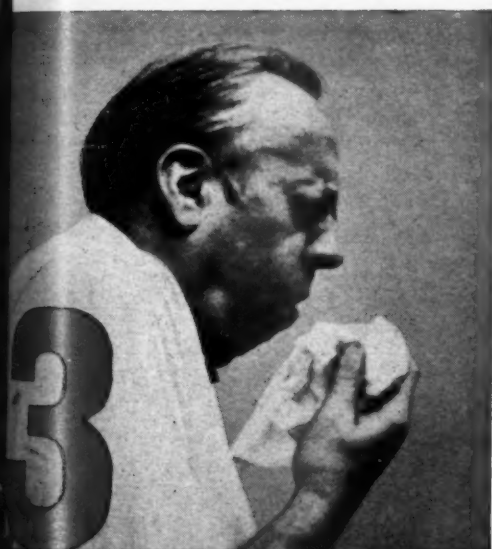
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(equivalent to 3.5 mg. neomycin base)	
Benzocaine	5 mg.



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FROM THE EDITOR'S NOTEBOOK

CARCINOMA OF THE BREAST: Twenty-five thousand deaths per year from cancer of the breast, or 10 per cent of all the deaths from malignancy, 25 per cent of all the cancer deaths in the female. In 6 to 10 per cent of them it will be bilateral. If the patient receives no treatment, 18 per cent will survive five years, 10 per cent six years.

At the time of surgery, 40 per cent will have the disease confined to the breast, 50 per cent will have axillary metastasis, 18 per cent distal metastasis. If the disease is confined to the breast, there is a 77 per cent five year survival, 45 per cent if there are axillary metastasis and only 11 per cent five-year survival if there are distal metastasis.

Local recurrence in 4 to 6 per cent of the cases, a figure not particularly altered by the thickness of the skin flaps. Operative mortality from radical mastectomy is 0.9 per cent.

At the University of Chicago they are noting in Stage I or where the carcinoma is confined to the breast, a radical mastectomy results in 75 to 80 per cent five-year survivals. This can be elevated to a 85 to 90 per cent five-year survival if it is combined with x-ray treatment. Other studies have not shown this increased cure rate with radiation in Stage I lesions. If the disease is in Stage II, or has axillary metastasis, they have a 46 per cent five-year survival with a radical mastectomy, with or without deep x-ray therapy. These results would make one wonder as to the advisability or desirability of deep x-ray therapy in any of the cases, in view of the frequency of radiation sickness and the increased incidence of lymph-edema if radiation is used in association with radical surgery.

Of the factors influencing prognosis:

1. If any lymph node is involved, there must be an overwhelming invasion of the nodes before there is a marked alteration in the five-year survival rate. As noted above, if no nodes are involved, a 77 per cent five-year survival is noted. Up to 20 nodes involved, a 63 per cent five-year survival. From 20 to 50 nodes involved, a 53 per cent five-year survival, and if over 50 nodes are involved, a 20 per cent five-year survival.
2. Age of the patient does not seem to be a statistically significant factor. In the overall

picture, no matter what the age, between 50 per cent and 57 per cent five-year survivals can be anticipated.

3. Duration of symptoms is of significance. If the symptoms are of less than one month duration, a 70 per cent five-year survival is noted. If it is more than six months duration, 56 per cent five-year survival.
4. Location seems to be a factor with the two areas presenting the poorest prognosis being a central lesion, or a lower inner quadrant lesion.
5. The most significant factor seems to be the size of the tumor. Under 2 cms. in size, 93 per cent five-year survival; 2-5 cms. in size there is a 60 per cent five-year survival; 5-9 cms. in size 47 per cent five-year survival, and if it is more than 10 cms. in size, a 10 per cent five-year survival.

In the postoperative period it can be anticipated that 25 per cent of those who will die of cancer will die each year during the first three years. That is, 75 per cent by the end of three years. Ten per cent will die after the sixth year, and under 11 years. Of those who survive five years, 70 per cent will be clinically free of the disease.

McWhorter's results with irradiation show only a 42 per cent five-year survival. Yet, the overall surgical statistics for radical mastectomy present a 56 per cent five-year survival.

The value of irradiation in cancer of the breast is of questionable benefit; so questionable that Dr. Regato will concur in its use only for focal irradiation and not field irradiation in the postoperative radical mastectomy patient.

The extended or supra-radical mastectomy as encouraged by Dr. Urban does not seem to increase the five-year survival rate.

Castration probably should be deferred until metastasis occurs and then it should be done surgically. Possibly adrenalectomy should follow castration. It is a formidable procedure with questionable results, in a limited group of patients, and at best helpful only for approximately nine months.

Aspiration of cysts seems to be a misleading procedure and probably all should be excised.

Needle biopsies are to be avoided. Metastasis along the line of aspiration is entirely too frequent.

Dr. Warren Cole has recently collected mate-

rial that shows 50 per cent recurrence if there is a delay between biopsy and radical surgery.

Dr. Ackerman would biopsy all doubtful lumps, for palpation of any nodule is inaccurate in 33 per cent of the cases. It is his feeling that a 1-to-2-day delay between biopsy and radical surgery does not alter the cure rate. The only extensive series reported is by Dr. Clagett who feels that the cure rate is cut by 25 per cent if there is a delay between the two procedures, and now Dr. Cole is stating that there is a detrimental factor of 50 per cent.

Gross examination at the time of surgery can only be accurate in about 85 per cent of the cases, for the confusing factors remain of a sclerosing adenosis, fat necrosis, fibrosis, and granular cell myoblastoma.

Physical examination of an axilla is notoriously erroneous. If no nodes are palpated, 50 per cent will be found to contain malignancy at the time of surgery. If nodes are palpated, 85 per cent will be found to be positive for malignancy at the time of surgery.

Paget's disease is the only skin lesion of the breast that starts on the nipple and extends to the areola. When it is biopsied, a segment of the nipple, areola and underlying duct should be removed.

If a breast lesion is in the upper outer quadrant and the axilla is negative for metastasis, there is almost a 100 per cent chance that the supraclavicular nodes and mediastinum will not show malignancy.

As to the supra-radical mastectomy, it is Dr. Ackerman's concept that dissection of the internal mammary chain is not particularly helpful. He outlines it in the following manner: If the first interspace is involved, it is hopeless. If all nodes or a high percentage of the nodes are involved, it is hopeless. If no nodes are involved, the procedure was useless. He analyzes Dr. Wangenstein's series of 64 patients with the extended radical procedure; there were eight deaths, 12.5 per cent mortality. Twenty-seven of the patients had negative nodes and consequently did not need the procedure anyway. Thirty-seven had positive nodes and of these, 25 are dead. Of the 12 who are living, six are living with disease. Of the other six, four are living less than two years. Of the remaining two, one has had irradiation, so one might attribute one survival to a procedure that has caused eight deaths.

As to McWhorter's series, Dr. Ackerman reviewed his five-year survivals which were the only cases McWhorter would permit to have reviewed. This included over 700 cases. It is Dr. Ackerman's feeling that radiotherapy was used in these cases in a rather "pugilistic manner," rather than "a once over lightly job." The x-ray was used as a cautery. Of the 700 survivals, 50 cases had severe irradiation effect. That is, approximately 7 per cent, and by severe irradiation effect is meant fractures, extensive sloughing and the necessity for amputations. It would seem to be a treatment that is attractive to the poorly trained surgeon only.

Dr. Ackerman further investigated 60 cases as to the possibility of killing cancer cells in breast tissue and found it an extremely difficult thing to do. Of the 60 cases, only seven were sterilized by irradiation and he feels it is quite debatable that malignancy can be sterilized or removed if it once exists in lymph nodes.

- 1—Dr. Garrett Allen—Prof. of Surgery, U. of Chicago.
- 2—Dr. Lauren Ackerman—Prof. of Pathology, Washington University, St. Louis.
- 3—Dr. O. T. Clagett—Mayo Clinic.
- 4—Dr. Warren Cole—Prof. of Surgery, U. of Illinois.
- 5—Dr. Juan Del Regato—Head of Fenrose Cancer Hosp.
- 6—Dr. J. A. Urban—Memorial Hospital, New York, N. Y.
- 7—Dr. O. H. Wangenstein—Prof. of Surgery, U. of Minnesota.

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WE GUARANTEE TO THE DOCTOR AND HIS PATIENT

LETTER TO THE EDITOR

Dear Editor:

FOR many years past I have been what might be termed an amateur student of medicine. I have also been interested more particularly in the organizations which have taken upon themselves the collection of monies to be devoted largely to the eradication of various diseases which still plague mankind.

Lately, this matter of raising funds for research looking to the cure of some dread malady has so intrigued me that I am seized with an uncontrollable desire to start a foundation of my own. I have an impressive roster of sponsors, including such well known names as James DeWitt Rockefeller, (local boy), Horace Pulham Whitney (an up country lad) and many more equally famous. I have had an impressive letterhead designed by a leading commercial artist. I have an exceptionally fine mailing list of persons in the upper income brackets.

My purpose in writing to you, gentlemen, is to plead for your assistance in one simple aspect of my plans, namely, won't you select a good disease for me? I have thought of beri-beri, pellagra, elephantiasis, trichinosis and many others, but when I look up the words in the dictionary, I always encounter some difficulty; the first three are tropical and I don't want to have to confine my efforts to the deep South. The fourth has something to do with pigs and certainly does not have the romantic urge so sorely needed for the success of a project of this kind. I rather

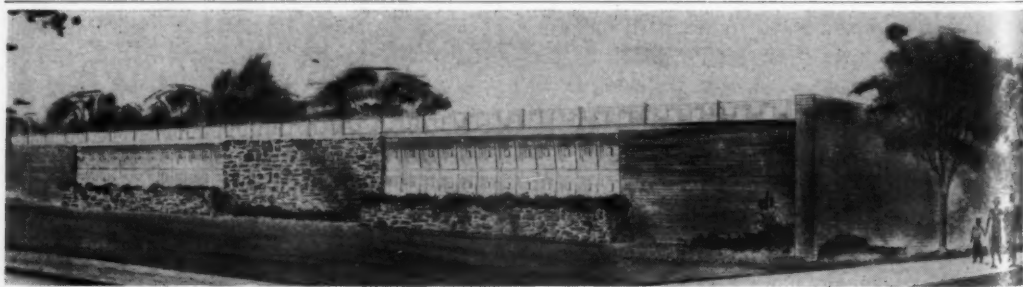
fancied leukemia, but only recently it was taken by another group. (I always thought it was a cancer of the red blood cells but I guess I was wrong.) Do you think that "Auricular and Ventricular Fibrillation" has possibilities? It has a beautiful ring to it, a sort of poetic, rhythmic cadence and even though it is only a mild heart condition, I doubt that many prospective donors would look it up.

But I shouldn't be expatiating on my own ideas when I intend to be guided solely by your good advice in the matter. Might I also suggest that you name an alternate, since by the time your letter arrives, the first selection may already be taken.

When I really have my organization in a sound financial position, I plan to underwrite what might be termed an auxiliary charity. With the continuing success of the Salk vaccine, there will undoubtedly be many people in that field without jobs and I propose insofar as possible to absorb them into my organization, thus avoiding a major unemployment problem.

It follows, therefore, that the ailments you suggest must present almost insurmountable obstacles to the research scientists, since I do not want them to arrive at a successful conclusion in a mere matter of a year or two. Such an unhappy contretemps would only necessitate a fresh start, all of which would be demoralizing to staff and contributors.

I await with anxiety your prompt reply. Thank you!



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Topics of Current Medical Interest

FINANCING MEDICAL EDUCATION

Harold Kohl, M.D.

A TOTAL of almost \$7 million has been raised by the American Medical Education Foundation and distributed to all of the medical schools in the United States since 1951. Although the total income of AMEF in 1957 was less than it was in 1956 by \$87,481, it is encouraging to note that the number of contributors has increased. In 1956 a total of 39,892 doctors contributed to medical education through AMEF while in 1957 the number was 44,155.

The Arizona Medical Association, one of the organizations receiving meritorious recognition in 1957, contributed \$9,113.50 as compared with \$4,897.87 in 1956. Of this amount, the Women's Auxiliary to the Arizona Medical Association is credited with \$600. The past year was the first in application of a \$10 dues increase noted by your house of delegates at its regular annual session in 1956, and earmarked for AMEF. A substantial number of members of the association contributed to medical education through AMEF over and above the \$10 dues increase, and many more sent monies for this purpose to their alma mater alumni associations. Most of those doctors who used AMEF as the channel for transmitted supplemental donations specified the medical school that was to receive the donation. *These gifts to medical education through AMEF reach the medical schools IN TOTO. Not one penny of any gift is spent for administration—the American Medical Association pays all expenses.*

Alumni fund contributions from Arizona doctors in 1956 were \$9,220. The figures for 1957 are not yet available. At some schools the alumni associations are contributing all unearmarked monies received for medical education through AMEF.

The unrestricted dollars which the deans of the medical schools receive from AMEF and the alumni funds are the most helpful things that have been done for medical education. Deans use the funds variously for long-overdue salary increases, needed equipment not available from budgeted money, and to finance trips to conferences which are sorely needed to boost the mo-

rale of faculty members who could not otherwise afford to attend. All undesignated gifts through AMEF are pro-rated to the 82 approved medical schools, of which at present 78 are four-year and four are two-year schools.

In the state of Arizona, as well as in every state in the Union, the driving force in raising monies for medical education is becoming more and more the women's auxiliary to the state society. It is difficult to overestimate the value of the efforts that our wives are making, and the stimulus that they have added to this outstandingly worthy project. In 1957, the Women's Auxiliary to the American Medical Association sent a check or checks to AMEF in the amount of \$133,540.56. These were not outright contributions but were the result of efforts which only the annual report of the women's auxiliary to each state association can clarify and outline.

Our own Jesse D. Hamer, M.D. of Phoenix, vice president of the American Medical Association 1957-1958, and advisory member to the American Medical Education Foundation, wrote an excellent article entitled, "Hippocratic Giving Through AMEF." This appeared in a recent alumni bulletin of the Western Reserve School of Medicine, and it is highly commended to your reading.

Another excellent article which every practicing physician in Arizona and in the United States and its possessions should read is, "Investment in Knowledge." This article appeared in the Journal of the American Medical Association, April 20, 1957, Vol. 163, and emphasizes the benefit that the deans of medical schools derive from the unearmarked funds which they receive chiefly through AMEF.

"I will look upon him who shall have taught me this Art even as one of my parents. I will share my substance with him, and I will supply his necessities, if he be in need. I will regard his offspring even as my own brethren, and I will teach them this Art, if they would learn it, without fee or covenant. I will impart this Art by precept, by lecture and by every mode of teaching, not only to my own sons but to the sons of him who has taught me, and to disciples bound by covenant and Oath, according to the Law of Medicine."

RX., DX., AND DRS.

Guillermo Osler, M.D.

HERE ARE three paragraphs on chest disease topics from a recent meeting in San Diego. Even if you are a nose-and-throater or an orthopod, they might be worth a glance. . . . Several medical groups combine their support and funds to present an afternoon-and-evening symposium there each year. It now has enlarged to about 300 physicians, and the naval hospital staff is the host group. . . . This year they had Drs. Holmes of Seattle, Harris of Los Angeles, Oatway of Altadena, Maddy (USPHS, DVM) of Phoenix, and Dr. Shaw of Dallas. Each performed twice during the day. . . . The following notes seemed to be either new or worth repeating:

1. **DR. SHAW** believes that it is legitimate not to do resection on closed negative disease with nodules. The few relapses which occur are treatable at once, and the major portion of the lung has been spared operation, as well as the major portion of the patients. . . . He said that he believed cavitative lesions should be resected between the fourth and sixth month after chemotherapy was started, in most patients. . . . "Isoniazid cysts" are hard to resect. He is not sure that they need operation; probably they do need resection when they occur in lower lobes, but not if bilateral. He recommended continuing chemotherapy and observation. . . . He believes that the open positive case should be operated, with all the protection of drugs possible. . . . He reminded the audience that thoracoplasty is not done to prevent over-extension but to obliterate space. . . . He quoted Ahlmstead, in one of the Scandinavian countries, who had experience with 3,500 cases which had tuberculous nodules in the past 10 years. There was a 2 per cent morbidity in his series, and a 0.05 per cent mortality. He believes that nodules may have to be taken out for industrial or economic reasons, and this also applies to "isoniazid cysts."

2. **Dr. Maddy** suggested that there is coccidioidomycosis infection in San Diego County, and that the skin-test incidence is 8 to 10 per cent at the age of 18 years. This means that 25 to 40 per cent of the people are infected during their lives. . . . All domestic animals can be infected, and probably are occasionally infected, as well as the animals in the San Diego Zoo. Dogs develop disseminated disease, but cattle do not develop disseminated disease. . . . **Pinal County in Arizona** has the highest incidence of cocc. infection in the world, and 100 per cent of the people living there develop a positive skin test within a year's residence. . . . A major factor in incidence is that the rainfall must vary between a range of nine to 25 inches per year. Minimal temperature in January should be around 40 to 50 degrees, and

the maximum temperature 80 to 90 degrees, with a mean in July of 68 degrees. Freezing will kill the coccidioides, but high heat is needed for their development. . . . The coastal belt about seven miles inland from the ocean in California is free of infection. Further inland for seven to 10 miles is an endemic area. It is variable, and is greatest in the desert areas.

3. **DR. HOLMES** suggested that mental depression is accompanied by a reduced adrenal function, and there is a coincident lowering of the 17-ketosteroid excretion. This is accompanied by slow healing, or a worsening, of tuberculosis disease. . . . Anxiety is not the same as depression, and it does not necessarily mean a spread, even with tension. Spreads occur only with the depression. . . . He suggested that stressful events can have an effect on adrenal function (and therefore on tuberculosis, etc.), and include marital upsets, social withdrawal, and economic strain. . . . He said that there was a definite difference between depression (or even agitated depression) and anxiety. The former is accompanied by hopelessness, while anxiety is accompanied by a feeling of danger and the need to do something, whether the person knows what to do or not.

Another step seems to have been taken in the progress toward a medical school for Arizona. President Harvill has indicated to the regents that the University of Arizona desires to proceed with a two-year school of medicine. The time for initiation of the proposal would be determined by the regents and consultants. . . . A two-year school is a logical way to start. Clinical facilities and faculty will follow along in sequence, just as they have in other cracking good schools, e.g. Colorado, Utah, Wisconsin, Kansas, etc.

MEDICAL ECONOMICS is a good but not unduly modest mag. They recently quoted a survey of about 27,000 M.D.s under 65 by Medical Publishing Research. They got replies from 9,132 on what journals were found **MOST HELPFUL**. Med. Econ. came first, by chance; JAMA second; Modern Medicine third, and others also ran. The question as to which was **MOST INTERESTING** also found the list headed by Med. Ec.; the new 'M.D.' was next; Modern Medicine was third; and the JAMA was in the money but fourth. . . . This should cause a storm on Dearborn Street, Chicago. . . . **ARIZONA MEDICINE** wasn't on either list, but that is because the research company is in Connecticut, and because they only asked questions about five journals. Just let 'em survey Arizona!

Maybe this is a cynical month, but the work of Malek and associates of Prague on lymphotropic antibiotics reminds us of a similar and forgotten

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drug. They believe that "antibiolymphins" (salts of certain antibiotics) are absorbed by the lymphatics and cause unusually high lymph levels. . . . The unfortunate similarity is to a type of penicillin which was said to concentrate in the respiratory tissue. . . . Maybe both trophic effects will become valuable as time goes on; then we will smile again.

A relatively NEW DRUG FOR ASTHMA is Elixophyllin, an alcohol-water solution of theophylline (the parent drug of amphylline). It is a palatable liquid which is given orally and is said to be absorbed from the stomach quite rapidly. It spells-off the ephedrine-containing drugs.

* * *

Manufacturers may combine drugs with the aim of synergism, additive effects, or of using one to decrease the toxicity or undesirable effects of the other. This makes some strange therapeutic bed-fellows. . . . 'Meproline' (Merck Sharpe and Dohme) now contains an Al HO gel to avoid that ulcer tendency. . . . 'Maredox' (Burroughs Wellcome & Co.) is made of a cyclizine and pyridoxine. You get the anti-nausea effect plus the counteraction of the tendency of Vit. B deficiency. . . . 'Achromatin V' contains tetracycline and nystatin, which Lederle hopes will suppress the monilia before they get started. . . . Another Lederle material is 'Pathibamate,' to take care of the "anxiety and tension in the GI tract." It has meprobamate, a well-known 'trankie,' and Pathilon which acts like belladonna. . . . Finally Lederle goes hog-wild in naming 'Falvin with Autrinic' for anemia. . . . 'Tridal' is a Lakeside product with obscurely named contents — Dactil and Piptal. They are said to be antispasmodic and anticholinergic. . . . Wallace Labs made 'Milpath' out of Miltown and 3-diethyl amino-1-dicyclohexyl-1-phenyl-1-propanol-ethiodide (which some printer will need for his indigestion after setting that one). . . . Wallace also uses Miltown plus conjugated equine estrogens to make 'Milprem,' an 'advance in menopausal therapy.' . . . Pfizer's contribution to combinations is 'Lindoxine,' a mixture of linoleic acid (essential unsaturated fatty acid) and pyridoxine (the Vit B₆ which is essential to the utilization of its colleague in the body). The purpose is modish, "to reduce elevated blood cholesterol, and to help minimize the development of atherosclerosis." . . . We still like the Oregon doc's "Pillapaprops," — pills which parallel the problem, and are made in layers which become available as the predicted need arises.

* * *

Hodgkin's disease may produce superior caval obstruction or spinal cord pressure. Diamond, of the N. Y. Memorial Center, has found that radiation will clear 50 per cent of such changes very rapidly (weeks), and RADIATION AND CHEMOTHERAPY will cause 90 per cent to regress with a similar speed which may begin within 12 hours.

. . . The duration? Don't ask.

* * *

There has been a (natural) tendency to sniff or raise an eyebrow when these endocrinology fellers talk about the effect of stress on body function. Selye has had an ingenious explanation, and we all use the term 'psychosomatic.' . . . Well sir, we now may have to compromise a bit more. They've begun to show us figures on stress and ketosteroid excretion. Also, Rosenman and Friedman have reported to the American Heart Association that unusual emotional stress and tension (in the seasonal work of accountants) has produced "significant increases of serum cholesterol and acceleration of the clotting time." . . . This could mean that alteration of diet in well persons may be ineffectual if stress is the major factor.

* * *

Swartwelder and Frye of LSU in New Orleans have announced that 'Dithiazanine' is a potent drug against four **INTESTINAL PARASITES**. It is used orally. Whipworms, strongyloides, large roundworms, and pinworms are destroyed. Hookworm is also affected, but their 400 cases do not yet show how much. . . . Millions of people have one or several of these infestations, chiefly in tropical countries, and the drug would be miraculous if it does 25 per cent of the claims.

* * *

A few more comments on **viral hepatitis** could be made in the interests of clarity. John R. Ewan of Washington helps a lot. . . . There are two types of disease. The **infectious hepatitis** is caused by virus A (the IH virus). The incubation period is two to six weeks, though carriers may have the virus for as long as 16 months. Infection occurs through food, water, or personal contact. . . . **Serum hepatitis** is caused by virus B (the SH virus). The incubation is one and a half to six months, and transmission is parenteral, by way of syringes, etc., though insects and sexual contact may be the mode. . . . The differential diagnosis of viral hepatitis is a lengthy study. . . . The morbidity lasts four months, but the mortality is only 0.5 per cent. . . . The condition was described in the eighth century, was rife in the Napoleonic and Civil Wars, was frequent in World War I, and of high incidence in World War II. Virus hepatitis (chiefly "infectious") was fifth most common in the USPHS reports of infectious communicable diseases in 1955. . . . Thank you, Dr. Ewan.

* * *

WE GOT LOST DEPARTMENT: The science of **VECTORCARDIOLOGY** slipped in while we were reading the Sat. Eve. Post one year. However, now that it is here we should be careful to have the best quality equipment. First you have to be able to talk the language, such as "having an instrument which will record hi-fidelity tracings of any scalar phenomena, such as stethophone, Frank Null probe, etc." . . . I refer you to the Hart Electronics Company of Pasadena for translation.

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DOCTORS IN AMERICAN POLITICAL LIFE

Five Doctors Signed The Declaration of Independence

IN 1776, Josiah Bartlett was 47 years of age, described by his biographer as "a tall man with a fine figure . . . who . . . wore his auburn hair in a queue." He was considerably more than that. He was a distinguished Massachusetts physician and an able and ardent patriot. He already had suffered for his interest in politics; he had been ousted from his post as justice of the peace by the royal governor of Massachusetts, and had seen his home burned to the ground.

By 1776 Dr. Bartlett clearly had made his choice. So it was natural that as a Massachusetts delegate to the Continental Congress he signed the Declaration of Independence. Perhaps it was only an accident, but he was the second person to sign the engrossed document at the formal ceremony on Aug. 2 of that year.

Dr. Bartlett was not the only physician to sign the Declaration. There were four others: Drs. Lyman Hall, Benjamin Rush, Matthew Thornton and Oliver Wolcott. All except Dr. Wolcott were in active practice at the time; while trained in medicine, he had given it up for law.

With all the others who signed the document—the lawyers, the statesmen, the soldiers, the business men—these five doctors were to achieve a degree of immortality. They are also symbolic of the strong interest the medical profession has taken in national legislation over the years.

Doctors In Congress Through The Years:

By States, By Parties

Dr. Bartlett had been one of four physician members of the Second Continental Congress in 1775. The next year the colonies sent eight doctors to the deliberations. In the critical years of 1783-84, 11 doctors were in the young congresses that struggled to keep the states united. It is a tribute to the versatility of the profession that in the 181 years since 1775, doctors have sat in every congress.

Research by the American Medical Association carries down through nearly two centuries,

congress by congress, the story of the medical profession's contribution to the development of the American legislature. Here are some statistics on the doctors' participation:

Total Representation: Six physicians now are members of the house of representatives of the 85th congress that convened in January. Counting them, a total of 359 physicians have served in American congresses since 1775, including 35 senators. Of the 359, 11 practiced another profession—generally law—as well as medicine, 33 were not active in practice when elected, and 18 had graduated in medicine, but never practiced.

By Parties: A total of 165 physicians were Democrats. Other party representation: Republicans, 67; Whigs, 30; Federalists, 17; Jacksonian Democrats, six; American Party, five; National Republicans, two; Independents, two; and one each from six other minor parties. There is no record of party affiliation for 32 doctors in congress, and party labels were not attached to the 27 who sat in the Continental Congress between 1775 and 1788.

By States: The large states that were members of the original 13 colonies naturally have supplied the most doctors to congress. Leading the list is Pennsylvania with 52. Next are New York with 48, and New Jersey, 30. Ohio, although coming into the Union later, has sent 26 doctors to congress. Other totals: Georgia, 17; Kentucky, 12; Maryland, 16; Massachusetts, 13; Missouri, 10; New Hampshire, 14; Virginia, 18; North Carolina, 11. Connecticut has elected six to congress, Delaware seven, Illinois five, Indiana seven, Louisiana five, Michigan five, South Carolina five, Tennessee eight. The following have elected from one to four physicians as representatives or senators: Alabama, Arkansas, California, North Dakota, Florida, Idaho, Iowa, Maine, Minnesota, Montana, Nebraska, New Mexico, Oregon, Rhode Island, Texas, Utah, Vermont, Washington, West Virginia, Wisconsin and Wyoming. Puerto Rico's present resident commissioner also is a physician, Dr. A. Fernos-Isern. He is a non-voting member of the house.

LEGISLATION COMMITTEE ACTION MENTAL COMMITMENT BILL

DOCTOR JEFFREY, "The delay in holding this meeting was based on the fact that the principle problem of legislation this year, the mental commitment bill, took a little longer to finally get completely redrafted and ready. The reason for this was that the medical association decided it was going to actually compile and rewrite this entire thing as a medical association project, rather than allowing the various and sundry groups of interested members of the mental health association to try to get together and work something out, which they probably could never do. As a result, starting last summer, and going all the way up through November, in fact half of December, Doctor Wick, Mr. Carpenter, and Mr. Jacobson, our legal counsel, met repeatedly and finally came up with what we think is a pretty good bill. Now as you folks know, this problem has been kicked around for longer than you really care to talk about and we met in this room last year and argued about a mental commitment bill. There were whole groups of things that legislators specifically objected to, and it was one of my uncomfortable jobs a year or so ago to go down to the legislature on its last night of session, as they were about to ram through a commitment bill, and tell them all I knew was that the medical association had never seen the bill that they were about to pass; and as a result nothing actually ever happened. Now, of course, the mental health associations were a little bit annoyed, but I think they were pacified for the moment. This bill has been culled out of all the various chapters (general health code of the state), with specific changes and very specific protection of individual rights. We think, or I should say Mr. Jacobson and his group that are working so hard on it, they think that all of the legislative objections that had been raised are eliminated in it. Now, I am sure someone is going to come up with some quibbling over some of the points. However, this present bill (tentative bill) has been reviewed by Judge Lockwood, Maricopa County Superior Court, president of the judges' association; and she herself went over this thing carefully and corrected some legal verbiage here and there and brought up a few points that superior court judges usually have trouble with, and she is taking it upon herself as

her own personal problem to get a specific approval of each individual superior court judge, so that when this bill, if and when presented to the legislature, we will have the backing of: (1) the medical association; (2) the psychiatrists; (3) superior court judges; and we trust the mental health association. Now, we have to do this a little bit backwards and I have to apologize for the timing element, but this tentative bill was presented to our own council before it was presented to the legislation committee. Now, this is backwards, and I know it, and there is nothing I can do about it, except that the fact was that the council was meeting in November and I wasn't sure exactly when they might meet again; and I wanted council to endorse this before the legislature actually convened. Council approved this basically and in principle as to the bill itself, subject to final approval by the legislation committee."

Doctor Jeffrey reviewed with the committee a summary of the mental commitment bill as prepared by Mr. Jacobson. Discussion ensued.

It was moved by Doctor Farness, seconded by Doctor Sprague and unanimously carried that we approve of this mental commitment bill for the submission for legislative action.

INDUSTRIAL RELATIONS COMMITTEE — INDUSTRIAL RELATIONS ACT—REVISION

Doctor Jeffrey read a letter addressed to him from the industrial relations committee dated Nov. 26, 1957, as follows: "The Industrial Relations Committee of the Arizona Medical Association, Inc., has been instructed by council of the association to call to the attention of the legislation committee certain sections of the Industrial Commission Act. Complaints of physicians have directed the attention of our committee to two particular sections of the Industrial Commission Act. The first of these is Section 59a, which provides that an employer or the employer's insurance carrier has the right to designate a physician in the case of an injured workman. There has been some feeling that this constitutes a contravention of the general medical principle of free choice of physician. The second section to which objection has been raised is that section of the act giving so-called elections in cases of employes injured through the negligence of a third party not in the employ of the employer. Election 2 under this portion of the act is so worded that it amounts to giving the industrial

commission fee schedule to private insurance carriers. It is to this specifically that objection has been made. I assume that your committee will proceed with independent study of these matters. If there is any assistance which can be given by the industrial relations committee or by me specifically as its chairman, please do not hesitate to call upon me." Signed, Lindsay E. Beaton, M.D., Chairman, Industrial Relations Committee. Discussion ensued.

It was moved by Doctor Farness, seconded by Doctor Hamer and unanimously carried that it is the opinion of this committee that: (1) this problem certainly bears deep investigation and possible future legislation; that it involves intrinsic problems within the industrial commission and its rule; and that Rule 59a is a rule and not a law; (2) the problem might consist of more or less a negotiated rule change rather than one of legislation; and (3) that the industrial relations committee should submit any proposed revision that suggests legislation.

PATIENT STERILIZATION — ARIZONA STATE HOSPITAL

By referral from council of this association the legislation committee considered the possibility of a change in the statutory requirements on sterilization of inmates at the Arizona State Hospital on petition of the superintendent and a hearing by the board of medical examiners. The question was raised by the board of medical examiners as to whether some more appropriate body might be designated to hold such hearings, and especially that such body include, among others, psychiatrists. Further, the possibility of obtaining for the board of medical examiners a reasonable appropriation from the state legislature to cover the expense involved in such procedures was discussed.

DOCTOR JEFFREY: "Shall we go along with this and offer no particular concrete proposal and so advise council?"

MR. CARPENTER: "Maybe we can confer with Doctor Wick and request him to prepare a program suitable to him for a referral in here." No action taken.

HR 250 (23RD ARIZONA LEGISLATURE) EDUCATION — USE OF SCHOOL MONIES

Doctor Jeffrey referred to a bill presented last year by Representative Holsclaw in the house of representatives, Arizona State Legislature (HR 250) regarding the use of school monies to pro-

vide medical and dental services for regularly enrolled school children in the public schools. Discussion ensued.

By motion regularly made and unanimously carried, the committee recommended to council that we should not endorse any legislation granting the use of school monies to provide medical and dental services for school children.

ARIZONA STATE DEPARTMENT OF HEALTH MEASURES

Doctor Jeffrey referred to several measures to be presented in the 23rd Arizona Legislature by the state department of health: (a) deficiency appropriations for the state tuberculosis sanatorium, (\$4,100 personal services); (b) deficiency appropriation for the state tuberculosis sanatorium (\$5,000 improvements); (c) establishing a division of mental health and appropriating funds; (d) prescribing functions of state department of health — regulation of semi-public swimming pools; (e) prescribing method of publication of proposed changes or repeals of regulations, and prescribing area in which board may make and amend rules and regulations; (f) providing for pure food control; (g) and declaration of public nuisances dangerous to public health—extentions. By motion regularly made and unanimously carried, the committee recommended to council that these are the internal affairs of the state health department and no action is called for at this time.

STUDY OF AIR POLLUTION PROBLEMS IN ARIZONA

It was reported that another bill to be presented the 23rd legislature would be to provide funds for the study of air pollution problems in Arizona.

Doctor McKhann, chairman, air pollution committee of our association, was asked to review this and give us his comments, which follow: "The proposed act relating to air pollution study and education of the state health department has been studied and discussed with several interested parties. It is my opinion that no harm can come from such an act and that much good may result, and I see no reason why the medical profession should not support it. Sooner or later we in Maricopa County at least must have more than study, if we want to keep our air clean, and some type of control will become a necessity. Ideally, it seems to me that study and control should be under the same general agency, else

study reports are apt to get lost and result in no action. If you have any further questions (I) shall try to answer them." Signed, George G. McKhann, M.D.

No action taken.

COMPACT FOR WESTERN REGIONAL CO-OPERATION IN HIGHER EDUCATION

The legislation committee was requested by the medical school committee to consider recommendations to: (1) reduce residency requirements under the WICHE program from 10 to five or less years; and (2) reasonably downgrade the financial repayment clause.

By motion regularly made and unanimously carried, the committee is favorably disposed to the recommendations of the medical school committee and that the education committees of the Arizona house and senate be so informed.

MATTRESS AND BEDDING RE-USE-PINAL COUNTY MEDICAL SOCIETY

By request of the component Pinal County Medical Society, the committee considered legislation regarding the re-use of mattresses and other bedding.

It was reported that Chapter 36, Paragraph 626 ARS 1956 refers to mattress and other bedding and directed that the Pinal County Medical Society be so informed, referring the matter to the state department of health. No further action indicated.

STATE MEDICAL EXAMINERS SYSTEM VS. STATE CORONERS SYSTEM

The question of a state medical examiners system versus existing state coroners system was again presented for consideration of the legislative committee. Discussion ensued.

The committee by motion regularly made and unanimously carried recommends to council the possibility of the State of Arizona undertaking a survey as to the need therefor.

ARIZONA POISONING CONTROL PROGRAM

Resolution No. 3, passed by the house of dele-

gates of this association on April 13, 1957, resolved in part that the need for legislation be determined and action taken by the committee on legislation toward providing legal requirements for the registration of toxic constituents and antidotes for all poisonous commercial products marketed in Arizona.

The committee by motion regularly made and unanimously carried, determined that this matter be referred to the board of health (state) for review and possible recommendation or suggestions as to how it should be done.

The committee reviewed the problem of lead poisoning from paint from children's toys. Since the manufacturer and importer of such toys has agreed to eliminate lead content finishes, no action seemed indicated.

PAUL R. HOFFMEISTER, PH.D.-PSYCHOLOGIST-PRACTICE OF HYPNOTHERAPY

At the request of Paul Singer, M.D., the committee studied the problem pertaining to the practices of a Paul R. Hoffmeister, Ph.D., a psychologist, reported to be practicing hypnotherapy.

The committee determined that this was a matter for investigation by the Board of Medical Examiners, State of Arizona. No action indicated.

HR 9467-85TH U. S. CONGRESS-HOSPITAL AND SURGICAL CARE (FORAND BILL)

Doctor Jesse D. Hamer, reported on the proposed HR 9467, Forand bill, in the 85th United States congress and the potential of such legislation. On direction of council of the association, the secretary has corresponded with all of Arizona's congressmen, expressing the views of the doctors of medicine in the State of Arizona. Both on the national level (AMA), and on the state and county levels an active vigorous campaign is indicated and being planned.

Leslie B. Smith, M.D.,
Secretary

By: Robert Carpenter,
Executive Secretary

PRESIDENT'S BUDGET AS IT RELATES TO HEALTH AND WELFARE FIELDS

THE PRESIDENT'S budget requests now are before congress for final decisions.

For the first time in many years, the President has asked congress to reduce a significant num-

ber of health-welfare appropriations. Also, Mr. Eisenhower hopes to set on a new course in federal-state relations; not only does he say that states and communities should shoulder more responsibilities in health and welfare fields — something that has been said often before — but he picks out specific areas where he believes the U. S. should reduce or end its activities.

PRESIDENT REQUESTS \$2.79 BILLION FOR HEALTH, EDUCATION, WELFARE

THE ADMINISTRATION wants \$2,794,412 to run all programs of the department of health, education, and welfare for the 12 months starting next July 1. This compares with \$2,747,717,212 in funds appropriated by the last session or to be requested in supplemental appropriations for the rest of this fiscal year. The new total planned, according to HEW Secretary Folsom, represents "sound and prudent investments in human resources" and "will make possible further progress in these fields."

President Eisenhower, in his budget message submitted Jan. 13, outlined a long-range plan for gradual reduction in grants-in-aid programs of the federal government and more reliance on the states. It would start with hospital construction, then spread to public assistance. Eventually vocational education and waste treatment plant construction would be turned over to the states. Under his proposals, some of the programs would be acted on this year, others considered in 1959 and 1960. Budget highlights follow:

Hill-Burton — With the authorizing legislation expiring June 30, 1959, and in view of progress already made toward meeting community hospital requirements for general beds, "the federal program should be modified to meet only the most urgent needs, with emphasis on specialized needs." For the next fiscal year, \$75 million is requested as against \$121 million for this year.

Public Assistance — U. S. spending for public assistance programs continues to mount. These programs are now well established and indi-

vidual states have gained experience on levels of assistance. Legislation will be submitted to gradually reduce federal participation in public assistance, effective in 1960. Total requested for next year: \$1,806,400,000, including unspecified amount for vendor medical payment.

Medical Research — Because of space-age emphasis on science, there would be additional funds for basic research in life sciences. Total spending for National Institutes of Health would remain at same level as current year, \$211,183,000, although there are some adjustments among the seven institutes.

Medical School Aid — Congress should enact legislation for federal construction grants to build medical school classrooms in order to aid in meeting medical and dental manpower needs. No money was requested. But for the laboratory research facilities program, the regular \$30 million is requested.

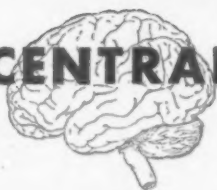
Social Security — "The rapid growth of federal programs for maintaining individual or family incomes and the numerous piecemeal liberalizations in the applicable laws suggest the need for appraising these activities as a whole. The advisory council on social security financing is studying some of the problems of retirement and disability insurance financing. . ."

Veterans' Administration — The President said he would send a message soon on changing compensation, pension and related programs for veterans because of fundamental changes in our society in the last several decades. In this connection the message notes the high proportion of non-service connected cases.

Food and Drug Administration — This agency would receive only 1 per cent more than the current year, or a total of \$10,664,500.

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NEW LEGISLATION IN CONGRESS

Tax Deductions . . . Veterans' Benefits . . .
Social Security . . . Proposed Conference
to Study Problems of Aged.

TAXATION — Rep. Boggs (L., La.) in HR 9633 would raise the limit on medical deductions for income tax purposes to permit disabled taxpayers over 65 and their spouses to take up to \$20,000 annually in deductions for medical expenses. . . . To help in financing education, Senator Frear (D., Del.) proposes to allow an additional exemption of \$600 per year for taxpayer, spouse or dependent while they are attending an institution of higher learning. Senator Frear's bill is S. 2938.

Additional exemptions for medical expenses also would be allowed for those qualifying as a student under this bill. The Frear bill is S. 2938. . . . A similar bill, HR 10026 by Rep. Sikes (D., Fla.), would allow an additional \$600 exemption for each child who is a student above the 12th grade. . . . In HR 9971, Rep. Ikard (D., Texas) would allow deduction from taxable income of money paid to institutions of higher learning for tuition, fees or books on behalf of the taxpayer or his dependents. . . . Rep. Teller (D., N.Y.) has the same idea in HR 10030, which would credit all additional expenses above the present \$600 exemption for taxpayer's dependent who is attending college.

Union Welfare Funds — S. 3044 by Senator Mundt (R., S. D.) proposes to require that union welfare funds (medical and hospital as well as pension, life, etc.) open their books for inspection by the treasury department's comptroller of currency. It would prohibit the National Labor Relations Board from acting on the complaint of any labor organization that could not certify that its books, and records, and those of its affiliated labor organizations, as well as its welfare plan, had been examined by the comptroller. The comptroller would be required to ascertain if the fund had been investing its money properly, and if its money was being administered for the purpose for which it was collected. If, after notification, the union did not discontinue the improper practices, the comptroller would be authorized to publish a report on the situation and to make the facts known to the appropriate law enforcement officer if there is evidence of law violation. The bill would re-

move the tax exemption of any union not meeting requirements, and any union employee found guilty of embezzlement would be subject to a \$5,000 fine or five years imprisonment, or both.

Veterans — A bill by Rep. Aspinall (D., Colo.) would extend from two to three years the period of presumption of service connection following separation for "chronic functional psychoses" and multiple sclerosis developing to a 10 per cent degree of disability. The presumption would apply for compensation purposes; under present law a veteran receiving compensation for a service-connected disability is entitled to hospitalization for that disability. The number is HR 9896. . . . Chairman Teague (D., Texas) of the house veterans' affairs committee in HR 10028 would forbid the veterans' administration to close any hospital, domiciliary home, medical center or regional office unless it gives his committee 90 days' advance notice. If a congressional session ends before the expiration of the 90 days, a new 90-day notification period would start at the opening of the next session. . . . Another Teague bill (HR 10029) would provide a two-year period for presumption of service connection for heart disease 10 per cent disabling; law now allows a minimum one year period for certain chronic diseases, including heart disease, unless by special legislation that period has been increased.

Rep. Rogers (R. Mass.) introduced HR 9717 as a means of technically correcting HR 1264, which passed the house last year and is pending in the senate. The objective is to grant the status of "permanently and totally disabled" for pension purposes to veterans suffering from active pulmonary tuberculosis while they are hospitalized. The latter bill was drawn up as an amendment to part of the VA statutes, which themselves were consolidated in the last days of the first session; the former bill corrects the statutory reference. . . . The consolidation mentioned above brought together all VA laws relating to compensation, pensions, hospitalization and burial benefits; Rep. Teague (D., Texas) is proposing to consolidate all VA laws and at the same time extend certain benefits to fringe groups, such as military cadets and national guard members while on inactive duty. The Teague bill is HR 9700. . . . Rep. Smith (D., Miss.) believes that if a veteran's condition has been rated as service-connected for 10 years or

more, he should have the security of a permanent designation of service-connection for the condition, even if in the meantime the condition has been rehabilitated. The Smith bill is HR 9726.

Social Security — A bill introduced by Rep. Roosevelt (D., Calif.) would increase the wage base on which social security taxes are collected from the present first \$4,200 of income to the first \$10,000. Also, the limit would go up \$500 each year that the consumer price index rises five points, and would remain at the higher level as long as any part of the index gain is retained. The monthly social security benefits also would be increased under a new formula. Under this bill a self-employed individual with an income of \$10,000 would pay at least \$637.50 in social security taxes alone. The number is HR 9834. . . . Mr. Roosevelt, in HR 9835, would make social security coverage compulsory for all physicians. . . . Another Roosevelt bill (HR 9836) would liberalize requirements for disability benefits both under the social security disability payments program and the disability "freeze" by a less strict definition of time the recipient has spent in covered occupations. It would make another important change by specifying that an applicant would be eligible for benefits if unable to obtain employment in an occupation similar to the work he formerly engaged in; under present law the benefit is allowed only if the applicant is physically unfit for any substantial gainful employment. Furthermore, a statement from a governmental agency that the applicant qualifies as disabled under its regulations would be sufficient evidence of disability under the social security program.

Rep. Fino (R., N.Y.) wants to raise the ceiling on income to be taxed under the social security system from the present \$4,200 to \$6,000 and increase OASDI monthly maximum payments to individuals from \$108.50 to \$138.50 and the maximum family payment from \$200 to \$250.

NEW REGULATIONS FOR PHYSICIANS WITH MEDICARE PATIENTS

OFFICE for Dependents' Medical Care has some new and clarifying regulations dealing with Medicare patients and ancillary medical personnel. They are:

Hospital Accommodations — Dependents are eligible for semi-private accommodations (two or more beds) and pediatric cases may be handled in wards. For private accommodations, the following should be kept in mind: (1) when this arrangement is believed necessary by the doctor, the patient pays 25 per cent of the difference between the private room fee and the weighted average of semi-private, (2) when the patient or sponsor only insists on private room, the patient pays the full difference, and (3) when the hospital has only private rooms, the Medicare patient pays 10 per cent of the daily charge for the room, or the total daily hospital charge, less \$15, whichever is the greater.

Independent Ancillary Personnel — Nurse anesthetists and physical therapists who work on an independent basis can now be paid direct if (1) the attending physician certifies on form DA-1863 that the services were authorized by him and (2) the amount charged does not exceed the normal charge to the public having an annual income of \$4,500.

Maternity Case Fees — If pregnancy terminates in premature delivery, the doctor is entitled to full fee if he has rendered continuous antepartum care beginning in the first eight weeks of pregnancy. Should a maternity patient consult a physician in a locality away from that of her attending doctor or clinic, the doctor consulted is entitled to fee for a home or office visit.

ADMINISTRATION OFFERS PAY RAISE BILL FOR VA MEDICAL PERSONNEL

THE VETERANS' administration has drafted and sent to congress legislation raising the pay scale of physicians and other personnel in the VA department of medicine and surgery. The administration proposal would raise pay in a range from 6 per cent to 18 per cent with the higher salaried getting the larger percentage

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increase. VA estimates its proposal would cost another \$10 million a year, as against \$6 million for a somewhat similar bill by Rep. Long (D., La.). Unlike the Long bill which is now pending in the house, the administration draft does not elevate optometrists to the same professional status as physicians within VA. In the last session, the VA indicated support of pay raises for medical personnel, but the budget bureau did

not favor the idea then. Meanwhile, a house veterans' affairs subcommittee has approved a bill designed to consolidate all VA laws and regulations, following consolidation last year of those dealing with compensation, pensions, hospitalization and burial benefits. Disabled American Veterans, Amvets, the Veterans of Foreign Wars and the American Legion all favor the bill.

PRESIDENT INVITES RUSSIA TO POOL MEDICAL EFFORTS

PRESIDENT Eisenhower wants Russia to join with the U. S. and other nations in a worldwide, co-operative effort to promote medical research and the control of diseases. In his State of the Union message, the President issued an open invitation to the Soviets to participate in the pooling of research skills to learn more about "diseases that are the common enemy of all mortals — such as cancer and heart disease." He also asked Russia to join in the campaign now under way, through the World Health Organization, "to eradicate from the face of the earth

that age-old scourge of mankind: malaria."

The President said: "If people can get together on such projects, is it not possible that we could then go on to a full-scale co-operative program of science for peace? . . . A program of science for peace might provide a means of funneling into one place the results of research from scientists everywhere and from there making it available to all parts of the world."

Mr. Eisenhower did not offer any framework around which to build the new program, presumably leaving the next step to Russia. His message did not mention any specific health objectives in domestic legislation, but he said subsequent messages would take up subjects not covered.

FEB. 1, 1958, PROGRESS REPORT FROM THE ARIZONA POISONING CONTROL INFORMATION CENTER AT THE UNIVERSITY OF ARIZONA COLLEGE OF PHARMACY

*National Clearing House for Poison Control
Centers Trade-Name Products Card File*

THE NATIONAL Clearing House for Poison Control Centers has provided the Arizona Poisoning Control Information Center with 443 trade-name product cards which provide information concerning toxic ingredients, degree of toxicity, clinical findings in poisoning, and recommended treatment. An additional 30 to 50 new cards will be received from the national clearing house each month. This information file will undoubtedly prove to be invaluable, since it considers only trade-name products that are not listed in toxicological and pharmacological references.

AMA Drafts Model Chemical Label Law

It is well-known that inadequate labeling of

potentially harmful chemicals has been a major handicap to a successful attack on the problem of accidental poisoning. The committee on toxicology of the American Medical Association has formulated a model law which, if adopted, would permit uniform legislation for the precautionary labeling of hazardous substances in commercial household and industrial chemical products. The law would (1) require labeling of all chemical products containing hazardous substances which are not now regulated, (2) require identification and warnings for strongly sensitizing chemicals which cause allergic or inflammatory reactions in living tissue on contact, (3) require the same labeling standards to apply to chemicals for export as those for domestic consumption, thereby obviating the common complaint that less-than-standard products are sold to foreign customers, and (4) prohibit re-use of food and drug containers bearing their original labels.

Notes on Promising New Antidotes

Penicillinase is a purified injectable enzyme obtained from cultures of *B. cereus* and is capable of inactivating circulating penicillin. It has been found especially useful in counteracting the allergic urticarial and serum sickness-like

reactions which may occur one hour to several hours after an injection of penicillin. The product does not act rapidly enough to protect those few patients who suffer immediate acute anaphylactic reactions from penicillin. The usual dose is 800,000 units, intramuscularly. It is available from Schenley Laboratories under the trade name, Neutrapen.

Megimide (B-methyl-B-ethyl glutarimide) (Bemegride) has been introduced into medical practice for the treatment of acute barbiturate intoxication and is at present the focus of much active clinical and pharmacological research. The drug accelerates considerably recovery of respiratory function, corneal reflexes, and oropharyngeal and somatic reflex responses. It has little specific effect on full recovery of consciousness, although it does diminish the depth of unconsciousness. The usual method of administration is either by slow intravenous infusion or by intermittent doses of 50 mg. each, with a time interval of three to five minutes. Recent studies with experimental animals have revealed that the drug is also effective against other central depressants such as glutethimide (Doriden) and various monoureides (Bromural, Carbromal). The drug is not at present available commercially in the United States, but has been made available for investigational use by Abbott Laboratories.

Methylphenidate (Ritalin) injectable has been found useful in reducing the respiratory depression and in elevating the severely lowered blood pressure of patients suffering from acute overdosage of barbiturates. Intravenous injection of 30 to 50 mg., repeated every 30 minutes, is recommended. Ritalin injectable is available in multiple dose vials from Ciba Pharmaceutical Products.

Penicillamine (B,B-dimethylcysteine) is a chelating agent which is being studied in Europe for the treatment of heavy metal poisoning. It is more effective than dimercaprol (BAL) and Edathamil calcium-disodium for treating hepatolenticular degeneration resulting from heavy metal toxicity. It has been shown to produce a rapid diuresis of copper, lead, and iron in poisoning with these metals, and, thus, should prove valuable in the treatment of heavy metal intoxications other than the one mentioned above. The drug is administered by mouth 0.3 gm. three times a day one-half hour before meals.

This dose has been administered for as long as 14 days with safety.

Cyanide Antidote Package: The efficacy of amyl nitrite or sodium nitrite, or their combination with thiosulfate in the treatment of cyanide poisoning has been confirmed experimentally and clinically. Eli Lilly and Company supplies a "Cyanide Antidote Package" which contains two ampuls sodium nitrite (0.3 gm. in 10 ml.), two ampuls sodium thiosulfate (12.5 gm. in 50 ml.), and 12 perles amyl nitrite.

Statistics of Thirty-Nine Poison Cases Reported Since the December 1, 1957 Progress Report

<i>Age:</i>	<i>Per Cent</i>
Under 5	71.8
6-15	5.1
16-30	10.3
31-45	5.1
Over 45	2.6
Unknown	5.1

Nature of Incident:

Accidental	92.3
Intentional	7.7

Outcome:

Recovery	100.0
Fatal	0.0

Time of Day:

Between 6 a.m. & noon	25.6
Between noon & 6 p.m.	45.8
Between 6 p.m. & midnight	13.3
Between midnight & 6 p.m.	5.1
Unknown	10.2

Causative Agents:

Aspirin preparations	36.3
Other medication (antibiotics, antihistamines, sedatives, & boric acid) .	10.1
Solvents (kerosene, paint thinner, etc.) .	7.6
Household bleaches	5.1
Cosmetics (perfume, finger nail polish, etc.)	5.1
Paint	5.1
Ornamental plants (castor bean)	5.1
Miscellaneous (shoe polish, wall plaster, insecticides, carbon tetrachloride, food poisoning)	25.6

when you encounter

- respiratory infections
- gastrointestinal infections
- genitourinary infections
- miscellaneous infections

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infections,
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1. Superior initial tetracycline blood levels—faster and higher than ever before—assuring fast transport of adequate tetracycline to the site of the infection.
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Supply:

Sumycin Capsules (per Capsule) 250
Sumycin Suspension (per 5 cc.) 125
Sumycin Pediatric Drops (per cc.—20 drops) 100

Tetracycline phosphate
complex equiv. to
tetracycline HCl (mg.)

Packaging:

Bottles of 16 and 100
2 oz. bottles
10 cc. dropper bottles

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IS MEDICINE IN THE "INSURANCE BUSINESS"?

MORE than 70 medical society-sponsored Blue Shield Plans are serving nearly one-fourth of the people of the United States, and underwriting about 40 per cent of all the basic surgical insurance and about 50 per cent of all the basic medical (non-surgical) insurance now in force. The rest is underwritten by more than 800 private insurance companies and independent local plans.

Is medicine — by its sponsorship and control of Blue Shield — in the "insurance business"? Let's remember, first, that the medical profession organized these Plans at a time when the insurance industry said it couldn't be done. And they were right. Medical care prepayment couldn't be organized and offered by an insurance company. It had to be done by medicine itself.

Blue Shield succeeded because America's doctors were behind it. They accepted less than normal schedules for their services; they agreed to accept (and in many areas they have actually accepted) pro-rated portions of those fees when the local Plan has been unable to pay the full schedule. Medicine's leaders have accepted the responsibility for guiding and directing their local Blue Shield Plans — a job that accounts for an incalculable number of unremunerated hours on the part of hundreds of the country's busiest physicians.

Have the members of the profession accepted these duties and responsibilities in order to put medicine "in the insurance business"? Certainly not! Medicine is in the business of providing medical care — nothing else. The profession has always been concerned with the ways and means by which patients pay for medical care and provide for future medical needs, and the profession quite naturally wants to control the basic economy of medical practice.

Medicine is *not* in the insurance business. But, through Blue Shield the profession *is* in the business of helping patients pay for their doctor's services. And in the final analysis, the patient alone profits through participation in Blue Shield.

R. R. RINEHART

LOCATION OPPORTUNITIES

Ashfork — Pop. 700 — North centrally located — Railroad center — Contact the Women's Club, Ashfork, Ariz.

Benson — Excellent opportunity for GP — This David-Benson trade area has about 5,000 population with only one doctor available. A small sleep-in hospital can be set up very easily. Hospital 25 miles away. Chamber of commerce will furnish telephone answering service, nine to five. Contact Bernard Fisher, D.D.S., Medical Committee of the Chamber of Commerce, Benson, Ariz., or James M. Hesser, M.D., 6th and Huachuca streets, Benson, Ariz.

Camp Verde — Located in the heart of a large farming and ranching area on the Verde River. Approximately 100 miles north of Phoenix. Badly in need of a medical doctor. Contact Ivy N. Moser, R.N., Camp Verde, Ariz.

Flagstaff — Pop. 17,500 — Largest city in the north central Arizona trading area. One pediatrician is needed (as there are a number of general practitioners who would gladly refer work to him.) Excellent opportunity for an EENT doctor and a general practitioner. Contact K. O. Hanson, M.D., Secretary, Coconino County Medical Society, 5 N. Leroux, Flagstaff, Ariz.

Gila Bend — Pop. 2,500 — 80 miles west of Phoenix — Nearest town to the Painted Rock Dam Project — Good opportunity for general practitioner. Cattle, cotton and general farming. Office and equipment available. \$150 monthly income from board of supervisors. Contact Mrs. J. F. Allison, Box 485, Gila Bend, Ariz.

Holbrook — Population above 7,000. Located in the heart of the northeastern pine country of Arizona on U. S. Route 66. Need services of general practitioner. For full details, contact Donald F. DeMarse, M.D., Box 397, Holbrook, Ariz.

Miami — Opportunity for GP — Industrial hospital staffed by approximately seven doctors, who care for personnel and families of those who work for the three principal mining companies. This community is served by numerous small mining and ranching interests. Contact Robert V. Horan, M.D., Miami-Inspiration Hospital, Miami, Ariz.

Morenci — Mining community located near New Mexico-Arizona border — Pop. 10,000 — Has vacancy at hospital for GP. Contact Carl H. Gans, M.D., Morenci Hospital, Morenci, Ariz.

Phoenix — Good opportunity for associate radiologist in Phoenix area. Contact Ernest Price, M.D., 9112 N. Second Street, Phoenix, Ariz. (WI 3-3491).

Safford — In need of GP — Pop. 6,000 — Has ideal year around climate with good schools, park, swimming pool, golf course, Elks Club. Private hospital, open staff. Surgical privileges after six months if qualified. Completely equipped office for rent and equipment for sale. Contact M. T. Sandeno, M.D., 803 Seventh Street, Safford, Ariz.

Show Low — Pop. 1,500 — Trading center for some 10,000 people. Summer and winter recreation area, cool climate and beautiful forest country. At present there is no M.D. in Show Low and it wishes to locate a doctor there who would help establish a hospital. The town is anxious to locate a doctor and promises full co-operation. Contact either Mary and Eric Marks, Paint Pony Lodge, Show Low, Ariz., or Donald F. DeMarse, M. D., Box 397, Holbrook, Ariz., or Mr. Mitchell Bushman, Show Low, Ariz.

Springerville — Need for general practitioner (private practice, to be associated with Doctor Browning). Good hospital facilities. Has drawing population of 6,000. Would like to obtain a doctor as soon as possible. Contact Ellis V. Browning, M.D., Box 390, Springerville, Ariz.

St. Johns — Seriously need a doctor of medicine, preferably a general practitioner, to locate in this east central Arizona community. Population is approximately 1,500 with several other small towns in the general area. About 20 miles from New Mexico in the beautiful rim country of Arizona. Contact Donald F. DeMarse, M.D., Box 397, Holbrook, Ariz.

Tolleson — In need of GP — Serves a trading population of from 12,000 to 15,000. Ten miles west of Phoenix. Elementary and high schools,

churches of all denominations. Complete office and equipment for GP available on reasonable term lease or purchase. Contact Mr. Peter Folbo, president, chamber of commerce, 9112 West Van Buren St., Tolleson, Ariz.

Tucson — The VA hospital is in urgent need of an orthopedic surgeon. They prefer someone who is board certified, but would take someone who has had special training, as they have the local men in this field available for consultation service. State license is necessary but not necessarily an Arizona license. Contact S. Netzer, M.D., director, professional service, VA hospital, Tucson, Ariz.

Youngtown — Pop. 130 — Located 16 miles from Phoenix and just a few miles from several small towns, each a potential field of practice. Most residents are 60 years of age or older and are in need of medical care. Office space is currently provided at no rental. A medical center is being planned. Interested doctors may contact Mr. Sid Lambert, Box 61, Marionette, Ariz.

FOR INFORMATION ON OPPORTUNITIES
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MEDICINE, CONTACT:

Harold J. Mills, M.D., Phelps Dodge Hospital,
Ajo, Ariz.

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THE UNEXCELLED
ANTIHISTAMINE

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Ira E. Harris, M.D., Miami-Inspiration Hospital, Miami, Ariz.

Charles B. Huestis, M.D., Box 928, Hayden, Ariz.

Elvie B. Jolley, M.D., Copper Queen Hospital, Bisbee, Ariz.

H. W. Finke, M.D., Magma Copper Company Hospital, Superior, Ariz.

John Edmonds, M.D., Kennecott Copper Corporation Hospital, Ray, Ariz.

Francis M. Finley, M.D., San Manuel Hospital, San Manuel, Ariz.

LOCATION INQUIRIES RECEIVED DURING MONTH OF JAN., 1958

BLENDERMAN, ALBERT D., M.D., 7244 Beverly, Overland Park, Kan.; Or; 1943 graduate of University of Vermont School of Medicine. Interned at the Beverly Hospital, Beverly, Mass., and is now completing an orthopedic residency at the VA Hospital, Kansas City, Mo. He is licensed in the state of Iowa and has served his military obligations. Desires clinic or associate type practice. Available July 1, 1958.

BOSSLER, DAVID W., M.D., Clinic Hospital, Shelton, Wash., GP; graduated from Northwestern University Medical School 1952 and interned at LDS Hospital, Salt Lake City, Utah. Is licensed in the state of Washington and holds national boards certification. Has completed his military obligations. Prefers clinic or associate

practice with opportunity for surgery and anesthesia. Available April or May 1958.

BURNSIDE, HOWARD B., M.D., 20403 Stratford, Detroit, Mich., R; graduated from Wayne University 1931 and interned at Henry Ford Hospital, Detroit. Has served residencies at Detroit Receiving Hospital and University Hospital, Little Rock, Ark. Is licensed in the states of Michigan, Illinois, Ohio and Arkansas. Is board certified as of 1955. Has completed his military obligations. Is available now.

CARROLL, C. WALLACE, M.D., 2838 South Ninth Street, Kansas City, Kan.; GP; 1957 graduate of the University of Kansas; interned at St. Mary's Hospital, Kansas City, Mo., and is licensed by the state of Kansas. Desires clinic or associate type practice. Available July 15, 1958.

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DROWSINESS AND OTHER SIDE EFFECTS.
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TICALS OF MERIT SINCE 1878



CASKEY, JOHN H., M.D., Second General Hospital, APO 180, New York, N. Y.; GP; is now working in the Army General Hospital and currently on active duty. Desires to leave military service and has completed his military obligations. Is a 1954 graduate of Baylor University College of Medicine and served his internship at the Brooke Army Hospital, San Antonio, Texas. Is licensed in the state of Texas. Is interested in group or associate type practice. Available July 1958.

CHAMBERS, WILLIAM R., M.D., 3053 Rodenhaven Drive, N. W., Atlanta, Ga.; NS; is a 1932 graduate of the University of Cincinnati Medical College. Served his internship at Cincinnati General Hospital and residencies at Hartford Hospital, Hartford, Conn., Henry Ford Hospital, Detroit, Mich., and the Lahey Clinic, Boston, Mass. Is a diplomate of the American Board of Neurological Surgery. Is licensed in numerous Eastern and Midwestern states. Desires clinic or associate type practice and is available now.

CHRISTIE, ROBERT WILLIAM, M.D., 11810 Seven Locks Road, Rockville, Md.; Path; is a graduate of the State University of New York, College of Medicine at New York City, 1951; and served internship at Hitchcock Hospital, Hanover, N. H. Is licensed in the states of Vermont and New York. All military obligations fulfilled. Desires group or associate type of practice, but also indicates interest in directing laboratories of several small rural hospitals. Available Oct. 1, 1958.

FAILOR, HARLAN JOHN, M.D., 427 Fourth St., S.W., Rochester, Minn.; I; is a 1954 graduate of the University of Wisconsin and interned at Detroit Receiving Hospital, Detroit, Mich. Is now serving residency at the Mayo Foundation in internal medicine. Is licensed in the states of Wisconsin and Minnesota. Service requirements are fulfilled. Desires associate practice and is available August 1958.

FARRAR, MAURICE C., M.D., 4222 Waban Hill, Madison 5, Wis.; ObG; is a 1953 graduate of the University of Wisconsin and interned at St. Joseph's Hospital, Phoenix, Ariz. Served residency training at Crawford W. Long Hospital, Atlanta, Ga. Desires clinic or partnership type practice and is available now.

GOLDSMITH, MELVIN LOWELL, M.D., 2929 S. Ellis Ave., Chicago 16, Ill.; GP; is a 1957 graduate of the University of Illinois and is now serving internship at the Michael Reese Hospital, Chicago, Ill. His military status has been deferred until June 1959. Desires clinic type practice and indicates interest for obstetrical and gynecology experience. Is available June 30, 1958.

HAGGAR, DAVID K., M.D., Hawarden, Iowa; GP; a 1943 graduate of the University of Nebraska; interned at Hurley Hospital, Flint, Mich. Has been practicing for past 10 years in Iowa.

Has completed his military obligations. Desires clinic or associate type of practice. Available June 1, 1958.

HOFFMAN, GEORGE TREYMANN, M.D., John Sealy Hospital, Galveston, Texas, NS; a 1944 graduate of the Marquette University School of Medicine, and interned at the Youngstown Hospital, Youngstown, Ohio. Is now finishing a neurosurgical residency at the John Sealy Hospital. Is licensed in the states of Wisconsin, Texas and California. Has fulfilled his military obligations. Desires clinic or associate type practice. Available July 15, 1958.

MERTZ, GEORGE H., M.D., Wayne County General Hospital, P. O. Box 211, Eloise, Mich.; GS, a 1953 graduate of the University of Colorado and served internship at Wayne County General Hospital, Eloise, Mich. Is licensed in the states of Colorado and Michigan. Is presently in fourth year of general surgery residency. Desires clinic or associate type practice. Is available July 10, 1958.

REEVES, HENRY GRAY, JR., M.D., University Hospital, Baltimore 1, Md.; S; is a 1951 graduate of the University of Maryland and is now finishing a surgical residency at University Hospital, Baltimore. Has completed his military obligations. Desires a clinic or associate type practice and is available July 1, 1958.

SKUDDER, PAUL ALBERT, M.D., 1300 University Ave., Madison, Wis.; S; is a 1953 graduate of the Cornell University School of Medicine and interned at the New York Hospital-Cornell University Medical Center, New York City. Is presently completing a residency in surgery at the University of Wisconsin Hospitals, Madison. Is licensed in the states of New York and Wisconsin. Has fulfilled his military obligations. Desires clinic or associate type practice. Available July 1, 1958.

STANDIFER, JOHN JAMES, M.D., 1972 Meadowbrook, Youngstown, Ohio; GP; a 1953 graduate of the University of Oklahoma School of Medicine and interned at Bremerton Navy Hospital, Bremerton, Wash. Is presently completing residency training in general surgery at the Youngstown Hospital Association, Youngstown, Ohio. Has fulfilled his military obligations. Desires general practice with associate. Available July 1958.

SULLIVAN, JOHN JOSEPH, M.D., 1122 North State St., Appleton, Wis.; ObG; 1945 graduate of the Loyola University Medical School. Interned at U. S. Naval Hospital, Long Beach, Calif. and received residency training in Lewis Memorial and Mercy Hospitals, Chicago, Ill. Is a diplomate of the American Board of Obstetrics and Gynecology and is licensed in several Midwestern states. Has fulfilled his military obligations. Desires associate type practice. Available May 1958.

TRIPP, RICHARD C., M.D., 1412 Plum St.,

Iowa City, Iowa; *OALR*; 1952 graduate of George Washington University. Interned at the Orange Memorial Hospital, Orange, N. J. and did residency training at University Hospitals, Iowa City, Iowa. Is a diplomate of National Board of Medical Examiners. Has completed his military obligations. Desires a two- or three-man specialty group or a clinic with all specialties represented. Available July 1, 1958.

VAN RIET, R. W., M.D., 412 15th Ave. Fulton, Ill.; *Ob-GP*; 1953 graduate of University of Amsterdam and interned at Englewood Hospital, Chicago, Ill. Is presently in general practice with emphasis on obstetrics. Prefers group type of practice and is available now.

WALLACE, EDWARD REILLY, M.D., 5201

60th St., Sacramento, Calif.; *GP*; 1954 graduate of Georgetown University. Interned at Sacramento County Hospital, Sacramento, Calif. and is licensed in California. Has fulfilled his military obligations. Desires a clinic or associate type of practice. Is available July 1, 1958.

WU, WILLIAM L. S., M.D., 245 Poplar Ave., Redwood City, Calif.; *I*; is a 1946 graduate of Stanford University; and interned at State University of Iowa Hospitals, Iowa, and Lincoln General Hospital, Lincoln, Neb. Instructor in internal medicine at Tulane University 1950-1954. Is licensed in the states of California and Louisiana. Has fulfilled his military obligations. Became a naturalized citizen 1955. Prefers clinic or associate type practice and is available now.

EXAMINATION PRIOR TO ISSUANCE OF MARRIAGE LICENSE

Opinion No. 58-9

Requested By: Arizona State Department of Health.

Opinion By: Robert Morrison, The Attorney General.

Question: What is required under ARS Sec. 25-103.01 for the issuance of a marriage license?

Conclusion: See body of opinion.

ARS Sec. 25-103.01 reads as follows:

"A. Before any person, who is or may hereafter be authorized by law to issue marriage licenses, shall issue any such license, each applicant therefore shall file with him a certificate from a duly licensed physician which certificate shall state that *the applicant has been given such examination, including a standard serological test, as may be necessary for the discovery of syphilis, made not more than 30 days or less than 48 hours prior to the date of issuance of such license, and that, in the opinion of such physician, the person either is not infected with syphilis, or if so infected, is not in a stage of that disease which is or may become communicable to the marital partner.*

"B. Any person who by law is validly able to obtain a marriage license in the State of Arizona is validly able to give consent to any examinations and tests required by this article. . ."

The intent of this legislation is to prevent the spread of syphilis in the community, and for the protection of the public welfare. *Ex Parte*

Woodruff, (1949) 210 P.2d 190, 197. Where a statute is plain and unambiguous there is no room for construction. *Automatic Registering Machine Company v. Pima County*, (1930) 36 Ariz. 367, 285 Pac. 1034; *State v. Borah*, 51 Ariz. 318, 76 P. 2d 757.

Under the terms of the statute, the applicant for a marriage license shall file with the person authorized to issue such license a certificate from a duly licensed physician.

The certificate from the physician must state:

1. That the applicant has been given an examination, including a standard serological test, for the discovery of syphilis.

2. The date of the examination.

3. That, in the opinion of the physician, the person:

- a. Is not infected with syphilis, or
- b. Is infected with syphilis but is not in a stage of the disease which is or may become communicable to the marital partner.

With respect to the extent of the examination by the physician, the only requirement of the statute, in addition to the serological test, is "such examination . . . as may be necessary for the discovery of syphilis."

The extent of the examination meets the requirement of the statute so long as it includes the serological test and enables the physician to certify that the person has been given an examination for the discovery of syphilis.

ROBERT MORRISON
The Attorney General

REPORT ON LEGAL ACTIONS AGAINST THE HOXSEY CANCER TREATMENT

By George P. Larrick

U. S. Commissioner of Food and Drugs

THE GOVERNMENT has now been successful in all pending federal court actions involving the "cancer remedies" known as the Hoxsey treatment.

At Pittsburgh, on Oct. 2, 1957, U. S. District Judge John L. Miller ordered the Hoxsey Cancer Clinic, Inc., of Pennsylvania to stop dispensing to out-of-state patients the Hoxsey treatment or any other drugs represented to be the Hoxsey treatment for internal cancer.

During the seven-day trial of this case, the government for the third time presented evidence that the Hoxsey treatment is worthless for internal cancer and results in harm to persons who rely upon it while neglecting to obtain competent medical treatment. Evidence was also presented that the Portage, Pa., clinic since last June had been treating out-of-state cancer patients with other simple medicines such as fig juice, vitamin pills, brewers' yeast tablets and anticid preparations, along with a prescription for saturated solution of potassium iodide. The latter is available without a prescription from any drugstore.

The Pennsylvania clinic and its officers agreed to drop their appeal from a previous jury verdict that the Hoxsey pills were falsely represented for cancer. They agreed to pay the \$14,000 costs in that case and to dismiss a suit in Washington, D. C., aimed at stopping further government investigations of the clinic.

We believe the Pennsylvania injunction will effectively stop interstate distribution of the Hoxsey cancer medicines from that state. Any action against distribution within Pennsylvania

will have to be undertaken by the state authorities.

At Washington, D. C., on Oct. 11, 1957, Federal Judge Alexander Holtzhoff dismissed a suit by Harry M. Hoxsey calling for withdrawal of a public warning against the Hoxsey treatment which has been displayed in U. S. post offices and other public buildings throughout the country. This suit alleged that the public information section of the Food, Drug, and Cosmetics Act was unconstitutional because there was no provision for a hearing before issuance of a public warning and this destroyed the plaintiff's business without due process of law. The court held that the law is constitutional and that even without specific statutory authority, the secretary of health, education, and welfare and the FDA had the right and the duty to warn the public in cases like this.

The FDA intends to seek vigorous enforcement of both the Pennsylvania injunction and the 1953 injunction issued by the federal court of Dallas.

The public should know, however, that such actions will not end the menace of this treatment, since the federal government does not have the power to stop a clinic in any state from treating cancer patients within that state with the nostrums which comprise the Hoxsey treatment. Millions of copies of false promotional literature are still in circulation; much of it reporting cures of persons who are now dead.

It is, therefore, of the utmost importance that cancer patients and their families who may be planning to try the Hoxsey treatment wherever it is available acquaint themselves with the facts about it. Again we urge all such persons to secure a copy of the public warning which was issued by the food and drug administration.

They may do this by writing to the Food and Drug Administration, Washington 25, D. C.

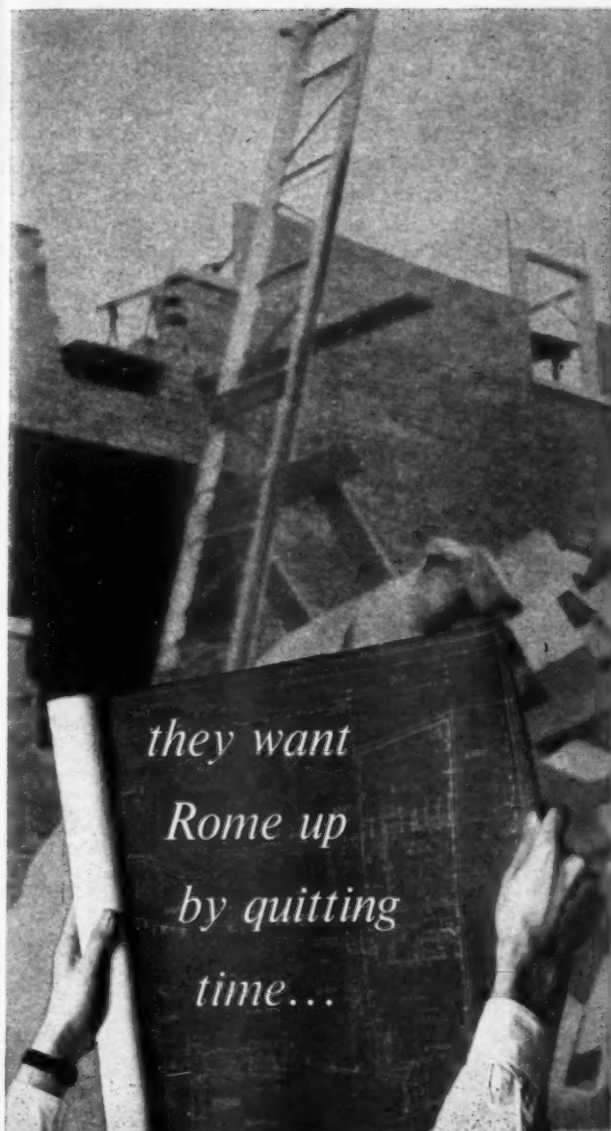
HOSPITAL EXPENSE INSURANCE

BENEFIT payments to persons covered by hospital expense insurance policies through the nation's insurance companies have increased more than 500 per cent since 1948, the Health Insurance Council reported today.

Designed to help pay for hospital bills, these benefits, according to the council have risen at a faster rate than the cost of hospital care

in the United States. During the period from 1948 to 1956, hospital charges have increased 125 per cent.

In a projection of 1956 totals reported by insurance companies writing health insurance policies, the council estimates that more than \$1 billion in benefits will be paid in 1957 under hospital expense insurance plans, as compared to some \$150 million received by patients confined in hospitals in 1948. During 1956 alone,



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¹ Comparative Effects of Various Rauwolfia Alkaloids on Hypertension Patients of the Chest, in press.

March, 1958

some \$900 million was paid in hospitalization benefits, added the council, a 500 per cent increase in nine years. These figures represent payments made to help cover the cost of hospital expenses only, and do not include benefits paid by insurance companies through other types of policies to cover the expenses of medical, surgical, and major medical care, and for loss of income expense insurance.

Evaluating the report, the council said that the "growth in benefit payments reflects both the greater proportion of hospital expenses being financed through insurance company policies, including practically every type of charge for hospital care, and the record expansion of these voluntary health insurance programs."

In this connection, the council noted that nearly 40 per cent, or over 8 million people, of the 21 million who entered a hospital last year had insurance company policies to help pay for the cost of illness or accident. By the end of 1956, a record 66.3 million Americans were protected against the cost of hospital care, both through individual and family health policies, and under group insurance programs. This represents a 155 per cent increase in the number of people thus covered since 1948.

In concluding its report of the rise in benefit payments in the last nine years, the council also noted that there has been a decrease in the time a patient remains in the hospital. According to the American Hospital Association, the average length of time in short-term general hospitals in 1948 was 8.1 days per patient. At the end of 1956, due to the advance in medical care and treatment, this average was reduced to 7.7 days.

AEC MAKES GRANTS FOR NUCLEAR TRAINING IN MEDICINE

SIX MEDICAL schools have received grants from the Atomic Energy Commission to help them obtain specialized radiation equipment and teaching aids. They would be used to stimulate study of radiobiology and uses of radioisotopes. This is the second group of grants in this field since October. The schools and their grants: University of Pittsburgh, \$25,520; University of North Carolina, \$15,100; University of Washington, \$12,600; Washington University, \$14,425; Vanderbilt University, \$15,000; University of Chicago, \$8,000.

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HEALTH AND THE SEXES

HEALTH INFORMATION FOUNDATION

WOMEN in the United States today live considerably longer, on the average, than men. In 1956, for example, the life expectancy of females at birth was over six years higher. In addition, the age-adjusted* mortality rate for males, 9.6 per 1,000 population, exceeded the corresponding rate for females by well over 50 per cent.

This better record of women results from the more rapid decline of their mortality since 1900, rather than from any increase in the death rate among men. While the male death rate dropped from 1900 to 1956 by almost one-half, the corresponding decline for females was much larger—just under two-thirds. The mortality differential between the sexes is now wider than at any time in the history of this country.

In 1900 the age-adjusted death rate for females stood at 17.0, while the corresponding rate for males, 18.6, was about 10 per cent higher. As the mortality for both sexes declined with time, the gap widened somewhat, only to narrow again immediately after the great influenza epidemic of 1918. Thereafter the long-term decline in mortality resumed, with women once again benefiting more from medical progress.

In 1956, there were 228,000 excess male deaths in this country — 896,500 deaths among males compared to 668,500 among females, according to preliminary estimates by the National Office of Vital Statistics. The annual differential has numbered over 100,000 since well before 1933 and over 200,000 since 1950. The excess would currently be even greater except that today many more women than men are alive at the older ages, when the mortality risk is greatest.

The extent to which females have benefited more than males from mortality decline varies widely by age. Even at the turn of the century males had a less favorable record than females at all ages, but the margin was not large throughout much of the life span. The excess was highest among infants—almost one-fourth; and at ages 35-64—about one-seventh.

The differential had widened considerably since that time at all ages except infancy and at 85 and over. (At these oldest ages there has even been a slight narrowing of the margin.) Currently, male mortality exceeds female by 140

per cent at ages 15-24, where the margin was formerly narrowest, and by 87 per cent at 55-64.

Disease Pattern Changes

Excess male mortality is characteristic of nearly all leading diseases; but the widening of the differential has, to a considerable extent, been associated with a shift in the leading causes of death, from the communicable diseases at the turn of the century to the degenerative diseases today.

In 1900 pneumonia and influenza, tuberculosis, and diarrhea and enteritis—three of the five leading causes of death, accounting for nearly a third of the total—resulted in excess male mortality of only 2, 9, and 9 per cent, respectively. By 1955 the importance of these diseases had declined; although their excess male mortality had risen sharply in the interim, their effect on the sex ratio for all deaths was almost negligible.

Heart disease in 1900 caused an excess male mortality of only 11 per cent. But after 1920 the differential rose steadily, reaching 78 per cent by 1955. This rise was associated with a decline in the infectious and rheumatic forms of the disease, and a corresponding increase in arteriosclerotic heart disease, especially diseases of the coronary arteries. Male mortality from heart disease is currently more than twice the female rate over the entire age range 35-64.

Because of the importance of heart disease in today's mortality picture (nearly 40 per cent of all deaths in 1956 were ascribed to this cause) a considerable proportion of the current excess of male deaths is accounted for by this disease alone. It causes more than half the total disparity at ages 40-74; thereafter the proportion declines, and is just under one-sixth at 85 and over.

At the upper ages, in addition to heart disease, malignant neoplasms (cancer) account for a sizable proportion of the excess male deaths. Cancer was a relatively minor factor in the mortality picture around 1900, causing about 4 per cent of all deaths. At that time female deaths from this disease exceeded male by 65 per cent. By 1955 cancer accounted for 16 per cent of all deaths, and there was an excess male mortality of 20 per cent.

The male death rate from cancer currently exceeds the female rate from birth through the ages of 25-29 and at 55 and over. After the early 20s, a large proportion of fatal malignancies involve the female breast and genitals.

*The age-adjusted death rate is used when mortality is compared over a period of years, because it allows for changes in age composition of the population.

At the older ages, the digestive system is the most common site, accounting for over 40 per cent of all cancer deaths. Males are most vulnerable, with their toll exceeding that of females by about 50 per cent at ages 60-74. The largest male excess in cancer mortality involves the respiratory system; the number of such deaths has increased spectacularly in recent years.

Male Accident Toll High

By far the highest excess of male deaths among the leading causes, especially at the younger ages, occurs among accidents. This cause alone accounts for over four-fifths of the excess male toll from all causes of death at ages 10-24, and nearly three-fourths at 25-34. The male excess is greatest—over 500 per cent—at 20-24. (Nevertheless, even if accidents could be eliminated as a cause of death, the excess male mortality would still be considerable.)

Accidents are unique among the leading causes of death in that the relative excess of male deaths, although still far larger than among the diseases, has declined since 1900. Much of this is due to the drop in importance of fatal work accidents, which take male lives almost exclusively.

Even before birth there is a pronounced difference between the sexes in the ability to survive. The fetal death (stillbirth) rate for males is 12 per cent higher than for females. The disparity rises to almost 30 per cent in the rate for deaths occurring within 24 hours after birth.

Prior to the present era of medical progress, maternal mortality was so high—about 20,000 in 1900* in the United States—that it represented a significant counterweight to excess male mortality. In addition, women often experienced the effects of childbirth years later in severe illness and impaired vitality, particularly when large families were the rule rather than the exception. But within recent years, maternal mortality has declined to such low levels—just under 1,600 in 1956—that it no longer represents a significant aspect of the problem.

Diabetes mellitus is the only major disease that has a higher age-adjusted mortality rate for women than men. The death rate from this disease, for reasons that continue to remain obscure, is over 35 per cent higher for females than males. Nevertheless, this has little effect on the total mortality situation, since in 1956 less than

2 per cent of all deaths were ascribed to this specific cause.

The sex difference in mortality now exists among all sectors of the population, although often in unequal degree. For example, among nonwhites, widening in the sex differential has lagged some years behind the rest of the population, although the general trend has been in the same direction. In 1956 the death rate for nonwhite males exceeded that for nonwhite females by 30 per cent, compared to a gap of over 60 per cent among whites. The shift from the communicable to the degenerative diseases as leading causes of death has been less widespread among nonwhites than among the total population.

Also, the larger the city, the wider is the differential mortality of its residents by sex. Thus, in a recent study* of mortality in New York State exclusive of New York City in 1949-51, the excess of male over female mortality within metropolitan areas varied from 39 per cent in central cities (population 50,000 and over) to 33 in other cities of 10,000 and over and 29 in places of under 10,000. Similarly, outside metropolitan areas, the percentages were 37 in places of 10,000 and over and 29 in places of under 10,000.

Social and economic class (based on occupation) is also associated with the magnitude of the sex ratio of mortality. In one study*, excess male mortality in England and Wales was higher between men and wives of men in professional and intermediate occupations, and lower for skilled, partly skilled, and unskilled occupations.

Morbidity Differences

The situation is quite different, and considerably more complex, with regard to illness. Women report themselves as ill more often than do men. Thus, in a series of periodic household surveys** of the white population by the United States Public Health Service, females reported 1,112 annual cases of illness (excluding female genital and puerperal causes) per 1,000 population, 20 per cent more than the 927 reported for males.

For disabling illness, i.e., illness in which the

*Data adapted from E. Parkhurst, "Differential Mortality in New York State, Exclusive of New York City, by Sex, Age, and Cause of Death, According to Degree of Urbanization," *American Journal of Public Health*, 46:959-965 (Aug. 3, 1956).

*Adapted from The Registrar General's Decennial Supplement, England and Wales, 1951, "Occupational Mortality, Part I," London, 1954.

**S. D. Collins et al., "Sickness Experience in Selected Areas of the United States," Public Health Monograph No. 25, Washington, D. C., 1955. These studies extended from the 1920's through the 1940's.

*Estimated by research department, Health Information Foundation.

patient is unable to conduct usual activities for one day or longer, and for bed cases, the situation was essentially similar: Higher rates were reported for females of 14 and 20 per cent, respectively. The excess of cases of chronic illness among females was particularly large — 54 per cent.

By age, the frequency of reported illness was higher among females at all ages past 10, with the highest excess, 60 per cent, at 45-54. These higher female rates spanned almost the entire range of diagnostic categories of illness.

Along with these higher morbidity rates, a study in Washington State in 1953 showed that women consulted physicians in private practice more often than did men, even omitting visits for purposes of health supervision or those connected with childbirth or conditions peculiar to the female sex.[†] Female visits exceeded those of males by 4 per cent, and this excess would have reached 10 per cent if there had been as many women as men in the population of that state. On the other hand, more U. S. males than females were hospital patients in 1953.*

The exact implications of these studies are not yet clear. For one thing, household surveys of illness are subject to various biases, including both under- and over-reporting, that may be selective for sex. Women, the chief respondents in these surveys, may be aware of, or remember, their own illnesses better than those of the men in their households. At the same time, economic and social pressure is undoubtedly greater on the breadwinners of the family—chiefly men—to ignore all but the most serious or disabling symptoms.

Studies of physicians in private practice omit a large segment of the physician population—for example, those associated with the veterans' administration, where men constitute a large majority of patients. And a census of hospital patients at a given time presents at best an incomplete picture, even of hospitalized morbidity, unless it includes data on admission rates and length of hospital stay. These are presently unavailable on a nation-wide basis in the detail required.

Long-Term Trends

The sex differential in mortality has left its mark on the population structure. In the early

years of the century, men enjoyed numerical ascendancy in this country in nearly all age groups. This situation resulted from the heavy influx of immigrants, among whom a sizable majority were males, as well as from the normal 5 to 6 per cent annual excess of male births.

When immigration diminished, however, while the annual excess of male deaths grew ever larger, the male population majority decreased and soon became a minority. Currently women outnumber men at all ages past the mid-20s.

The excess is particularly large—over a million in 1956 and increasing steadily—among persons aged 65 and over. By 1975, if present trends continue, this excess will have risen to 3¼ million; women will outnumber men by 138 to 100. Even at midlife—45-64—women will exceed men by 2.2 million, or 11 per cent.

Excess male mortality is by no means peculiar to the United States. Rather, it is common, with only minor exceptions, throughout much of the world. In general, the differential is greatest where life expectancy is highest, and widens as each country's mortality rate declines.*

Research currently seeks to determine whether the sex differential in mortality is due to biological or social (including environmental) factors. It is difficult to imagine that the disparity during the prenatal and neonatal periods, infancy, and even early childhood can be the result of social factors, since the environment of the sexes differs not at all or little during this period. Even during adulthood, Madigan** has made a strong case for biological causation by demonstrating significant differentials in the mortality experiences of men and women subject to almost identical environments. Implied is a greater constitutional resistance to degenerative disease on the part of women, which benefits them increasingly as the communicable diseases and hazards of maternity come under tighter control.

Nevertheless, the social environment unquestionably has a significant role in causing excess male mortality, especially from accidents. Also, the higher mortality differentials by sex in the larger cities and in the upper occupational groups suggest that certain modes of living may place an unequal stress on males. Perhaps men more than women are subject to internal stress,

[†]Data adapted from S. Standish, Jr., et al., *Why Patients See Doctors*, University of Washington Press, Seattle, 1955.

*F. G. Dickinson, "Age and Sex Distribution of Hospital Patients," Bulletin 97, Bureau of Medical Economic Research, American Medical Association, Chicago, 1955.

*United Nations, "Age and Sex Patterns of Mortality," Population Studies No. 22, 1955.

**F. C. Madigan, "Are Sex Mortality Differentials Biologically Caused?" *The Milbank Memorial Fund Quarterly*, XXXV, 2:202-223 (April) 1957.

with a consequent higher incidence of coronary artery disease and ulcers. Exercise or the lack of it, smoking, changing dietary habits, the propensity of women to take greater advantage of medical facilities—all these have been suggested as possibly related factors. But whatever the reasons, it would be well to concentrate medical research upon this problem before American males—especially those at age 45 and beyond—become in effect an underprivileged segment of the population.

NATIONAL FOUNDATION FOR INFANTILE PARALYSIS OFFERS FELLOWSHIPS FOR TISSUE CULTURE COURSE

THE National Foundation for Infantile Paralysis is again offering fellowships to postdoctoral investigators, teachers, graduate students and experienced laboratory personnel with the baccalaureate degree for participation in short courses in tissue culture.

Fellowships may be used for study only in formal courses designed to teach the principles, techniques, and application of tissue culture. Funds will be awarded for the period necessary to complete the course, which, in most instances, is not expected to exceed six weeks.

Financial assistance, based on individual need, may include an allowance for maintenance, for tuition and fees and for round-trip transportation.

Further information and application forms may be obtained from the Division of Professional Education. Completed application should reach the national foundation at least six weeks prior to the beginning of the course.

Write: Division of Professional Education, National Foundation for Infantile Paralysis, 301 E. 42nd Street, New York 17, N.Y.

BASIC COURSE IN ELECTROCARDIOGRAPHY

(Prerequisite to Advanced Course) Monday Through Saturday, March 31-April 5, 1958. Room 120, University of Oklahoma Medical Center, Oklahoma City, Okla.

This Course Will be Conducted By:

Robert H. Bayley, M. D., Professor of Medicine.

Loyal L. Conrad, M. D., Assistant Professor of Medicine.

T. Edward Cuddy, M. D., Fellow in Cardiology.

Mrs. Jean M. Tucker, Research Assistant.

General Description:

Presentations assume no formal acquaintance with the subject. The essential physical basis of the subject is emphasized throughout. All working materials are furnished. There will be daily practice sessions and review.

Enrollment limited to 30 physicians. This course is preparatory to the advanced course which emphasizes the clinical application of electrocardiographic theory and is offered in alternate years.

SCHOLARSHIP FOR TRAINING IN WORK WITH THE CEREBRAL PALSIED

SCHOLARSHIPS for advanced specialized training in work with the cerebral palsied are available under a program sponsored by Alpha Chi Omega, National Women's Fraternity, and the National Society for Crippled Children and Adults, Inc. Such training for doctors is available at the following places:

Cook County Graduate School of Medicine
707 South Wood Street

Chicago 12, Ill. Meyer Perlstein, M. D.

Children's Rehabilitation Institute

Reistertown, Md. Winthrop M. Phelps, M. D.

Postgraduate Cerebral Palsy Courses

Columbia University

College of Physicians and Surgeons

630 West 168th St.

New York 32, N. Y.

Any members interested in such a scholarship should write direct to the National Society for Crippled Children and Adults, Personnel and Training Service, 11 South La Salle St., Chicago 3, Ill., before April 1, 1958.

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Future Meetings

AMERICAN ACADEMY OF GENERAL PRACTICE

THE American Academy of General Practice 10th Annual Scientific Assembly, March 24-27 in Dallas's Memorial Auditorium.

The scientific program will feature 35 prominent physician-authorities. Ninety scientific and 300 technical exhibits will be prepared for the 7,000 doctors and guests expected to attend.

ILLINOIS STATE MEDICAL SOCIETY SPONSORS POST AMA MEETING HAWAIIAN TOUR

A WONDERFUL, colorful trip to the Hawaiian Islands has been planned in connection with the annual meeting of the American Medical Association in San Francisco in June. The journey will be sponsored by the Illinois State Medical Society for the benefit of its members and their families, but other physicians and their families are being invited to join the group.

The party will leave by air from San Francisco the night of June 26 and arrive in Honolulu the following morning.

For physicians who wish to learn something about medicine in the Islands there will be a Hawaiian summer medical conference in Honolulu, July 1-3.

Participants in the tour will leave Honolulu July 5, and have the option of returning to the mainland overnight by air, or on the luxurious air-conditioned SS Lurine. Those taking the boat will be treated to five days of additional enjoyment, and arrive in Los Angeles, July 10.

The trip can be made for as little as \$533. A descriptive brochure, with complete information, may be had by writing to Mr. M. W. Moloney, vice president of the Harvey T. Mason Travel Company, Inc., Professional Building, "Old Orchard," Skokie, Ill.

THE AMERICAN CONGRESS OF PHYSICAL MEDICINE AND REHABILITATION

THE 36th annual scientific and clinical session of the American Congress of Physical Medicine and Rehabilitation will be held Aug. 24-29, 1958

inclusive, at the Bellevue Stratford Hotel, Philadelphia.

Scientific and clinical sessions will be given Aug. 25, 26, 27, 28, and 29. All sessions will be open to members of the medical profession in good standing with the American Medical Association.

Full information may be obtained by writing to the executive secretary, Dorothea C. Augustin, American Congress of Physical Medicine and Rehabilitation, 30 North Michigan Ave., Chicago 2, Ill.

CYTOLOGY AND CANCER OF THE CERVIX

IN THIS brief pamphlet of 12 pages by the American Cancer Society, the rationale, the method, the reason, the potential results are given, which establish why the cervix should be studied cytologically. The references are in large part, classic, basic material on this subject which are valuable for clinicians and pathologists alike. The chart on follow-up procedures, on the inside back cover, is presented in the interest of thoroughness in the use of the method and practical guidance in circumstance of symptoms and/or positive or suspicious smears.

This pamphlet is readily available upon request from the Arizona division of the American Cancer Society.

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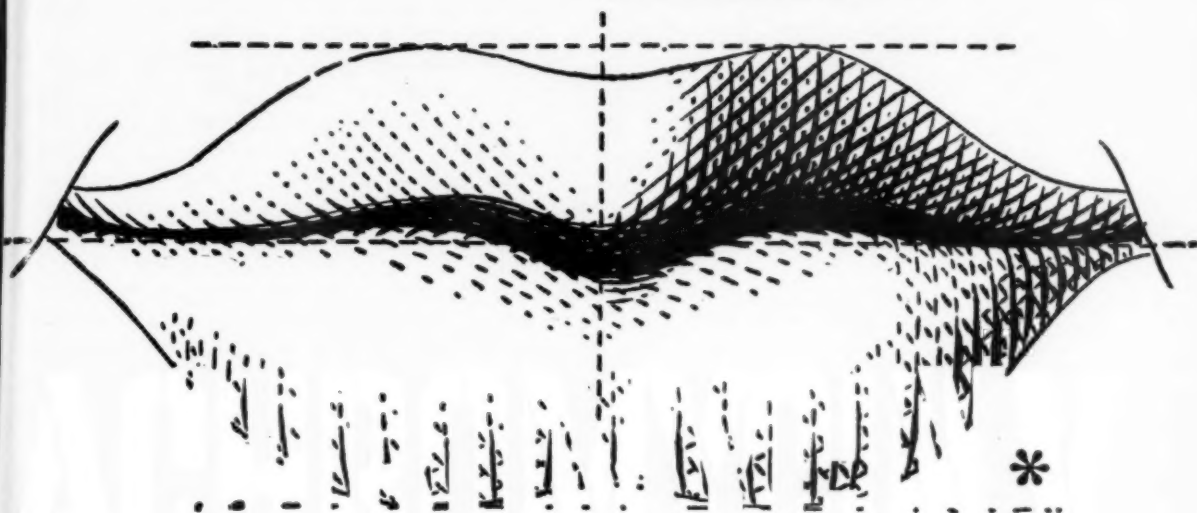
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The Case History in this discussion is selected from the Case Records of the Massachusetts General Hospital, and reprinted from the *New England Journal of Medicine*. The discussant under Differential Diagnosis is a member of the staff of the Massachusetts General Hospital. The other discussants are members of the Phoenix Clinical Club.

MASSACHUSETTS GENERAL HOSPITAL

PRESENTATION OF CASE 43162

A 58-YEAR-OLD woman entered the hospital because of loss of weight.

She was said to have had "nephritis" with albuminuria during two pregnancies 21 and 32 years previously. Both pregnancies terminated with stillbirths. Fifteen years before admission, a subtotal gastrectomy and posterior gastroenterostomy were performed because of a long standing duodenal ulcer that failed to heal with medical therapy. Physical examination at that time revealed a blood pressure of 148 systolic, 100 diastolic. The urine gave a three-plus test for albumin; the sediment contained an occasional red cell and 10 to 30 white cells per high-power field.

Examination of the blood showed a hemoglobin of 11.8 gm per 100 ml. and normal white-cell counts. The nonprotein nitrogen ranged between 42 mg. and 56 mg. per 100 ml. X-ray films demonstrated a dense, granular appearance of the bones of the spine and pelvis; punctate calcifications were seen to the right of the first lumbar vertebra. Subsequently, the patient felt well except for nocturnal episodes of generalized pruritus and epigastric fullness after large meals. One year later, an upper gastrointestinal series showed thickening of the mucosal folds of the remainder of the stomach; there was prompt passage of the barium through the stoma into a normal-appearing jejunum. The phenolsulfonphthalein excretion was 19 per cent after 30 minutes and 49 per cent after one and a half hours. The hemoglobin was 6.8 gm. per 100 ml. The nonprotein nitrogen was 44 mg. per 100 ml. After two transfusions of blood, the hemoglobin rose to 10 gm. per 100 ml.

Nine years before entry she noted postprandial mid-epigastric burning that occurred about twice weekly and occasionally at night. Physical examination showed the left border of cardiac dullness to extend 10 cm. to the left of the sternum. An upper gastrointestinal series showed no change from the previous examination except for failure of the afferent loop of jejunum to fill with barium. A Graham test was negative.

One year later an upper gastrointestinal series demonstrated a normally functioning anastomosis; increased density of the bones with coarsening of the trabecular pattern was noted. Six years before admission, the blood pressure was 160 systolic, 80 diastolic. The urine gave a one-plus test for albumin; the sediment contained a rare red cell and white cell per high-power field. The phenolsulfonphthalein excretion was 10 per cent in 30 minutes and 33 per cent after two hours. The hemoglobin was 13.2 gm. per 100 ml. The non-protein nitrogen was 60 mg., the total protein 6.5 gm., the albumin 4.5 gm. and the globulin 2 gm. per 100 ml. Mild symptoms of the "dumping" syndrome were treated with atropine and belladonna. Otherwise, the patient felt well and continued to work in a factory.

Between four and two years before admission, she noted gradually increasing pruritus of the arms and legs as well as a loss in weight from 115 to 107 pounds. Two years before entry, physical examination showed no change. The blood pressure was 160 systolic, 96 diastolic. The urine concentration test showed specific gravities of 1.010, 1.011 and 1.010. The phenolsulfonphthalein excretion was less than 5 per cent in 30 minutes and less than 20 per cent after two hours. The hemoglobin was 11.4 gm. per 100 ml. The nonprotein nitrogen was 88 mg., the total protein 5.7 gm., the albumin 4.1 gm., the globulin 1.6 gm., and the bilirubin less than 0.2 mg. per 100 ml. The alkaline phosphatase was 25.1 units. Bromsulfalein retention was 1 per cent, and cephalin flocculation was negative.

Stool specimens were normal. There was no steatorrhea. Subsequently, she felt well except for occasional epigastric distress and postprandial fatigue. The weight gradually fell to 91 pounds in spite of a good appetite. During the several months before admission, she noted pain in the thoracic spine, with rounding of the shoul-

ders and a loss of several inches in height, and pain and swelling of the left knee. She drank large quantities of milk during the two months before entry.

Physical examination showed a very thin, alert woman in no distress. Ophthalmologic examination revealed a white deposit in the paralimbal regions of both corneas. The heart was enlarged to the left. A Grade 3 apical systolic murmur was audible over the precordium. Examination of the abdomen was negative except for a surgical scar. The left knee was swollen, erythematous and warm; its motion was normal. There was no edema.

The temperature was 98.4°F, the pulse 84, and the respirations 20. The blood pressure was 170 systolic, 95 diastolic.

The urine gave a one-plus test for albumin; the sediment contained three red cells, eight white cells and numerous bacteria per high-power field. The concentration test showed specific gravities of 1.009, 1.012 and 1.012. The urinary calcium was 52.7 mg., and the phosphorus 510 mg. per 24 hours (total volume, 1,700 ml.). The creatinine clearance was 21 liters per 24 hours. Examination of the blood revealed a hemoglobin of 10 gm. per 100 ml. and a white-cell count of 5,000. The nonprotein nitrogen was 81 mg., the total protein 5.8 mg., the albumin 4 gm., the globulin 1.8 mg., the calcium 11 and 11.7 mg., the phosphorus 6 mg., the fasting blood sugar 90 mg., the creatinine 3.6 mg., the uric acid 6.1 mg., and the cholesterol 241 mg. per 100 ml. The potassium was 4.5 milliequiv., and the carbon dioxide 18 milliequiv. per liter. The prothrombin content was 82 per cent. The alkaline phosphatase was 43.8 and 63 units.

Stool specimens were dark brown and formed and gave negative guaiac tests; there was a normal amount of neutral fat; soaps and other fat combinations were increased (three plus); no undigested muscle fibers were seen. X-ray films of the chest demonstrated cardiac enlargement. Films of the upper spine showed moderate kyphoscoliosis with a dense, coarse, granular pattern of the thoracic vertebrae; the abdominal calcifications noted in previous films were in the same location. Films of the knees demonstrated some degenerative changes; the mineral content of the bones was good. Dental films showed the teeth to be in good condition; no lamina dura was identified.

With Amphojel and a low-carbohydrate, low-

calcium diet without added salt there were no gastrointestinal symptoms, and the weight remained about the same. The pain and swelling in the left knee subsided.

An operation was performed two months after admission.

HOWARD C. LAWRENCE, M.D.

It is my belief that a physician dealing with medical diagnosis each day would be moderately stressed in making the diagnosis of the case under discussion; a surgical clinician would find it difficult; I, as a practitioner of one of the so-called minor surgical specialties, find it almost impossible.

The long-standing history of kidney disease, including "nephritis" during two pregnancies, a gradually increasing NPN, gradually rising blood pressure, constant albuminuria, etc., is consistent with a diagnosis of chronic nephritis with renal insufficiency. Because there is no history of recurrent febrile episodes, I believe the diagnosis is chronic glomerulonephritis rather than chronic pyelonephritis.

Associated with this chronic renal disease, the patient has hypertension, cardiac enlargement, steadily deteriorating renal function as shown by repeated PSP tests, increasing NPN, elevated blood phosphorus, creatinine, and uric acid. I also believe that she has calcinosis (evidenced by the corneal calcific deposits and the punctate calcifications seen to the right of the first lumbar vertebra).

From the laboratory standpoint, the patient has a recurrent anemia, numerous evidences of azotemia, a gradually increasing alkaline phosphatase, no gross liver disease, normal or slightly elevated blood calcium, a high blood phosphorus, a low urine calcium and a high urine phosphorus. In addition, to the diagnosis of chronic glomerulonephritis with real insufficiency, calcinosis, hypertension, anemia and cardiac enlargement, there are numerous other diagnoses which will have to be considered; these include: Burnett or milk-alkali syndrome, renal osteodystrophy, primary or secondary hyperparathyroidism, and hyperparathyroidism producing secondary renal changes with insufficiency.

In 1949 Burnett and his associates described six cases of a new syndrome characterized by hypercalcemia without hypercalciuria or hypophosphatemia, with calcinosis, ocular lesions and renal insufficiency following prolonged intake of milk and alkalis in the treatment of peptic ulcer.

All of these cases demonstrated a normal serum alkaline phosphatase and a mild alkalosis. In each instance there was improvement on an intake low in mild and absorbable alkali. It is to be noted that the protocol indicates a long-standing history of upper gastro-intestinal disease requiring partial gastrectomy at the age of 43; it also states that she had drunk large quantities of milk during the two months before entry. Some of the historical data supports the diagnosis of milk-alkali syndrome; however, our patient has an acidosis rather than an alkalosis and there is marked elevation of the alkaline phosphatase. I do not believe this diagnosis is a tenable one.

In June 1956, Atlas et al., reported their doubts that some of the cases reported as milk-alkali syndrome were properly diagnosed. They felt that in some instances the diagnosis of hyperparathyroidism was the proper one. Kyle, in 1954, published an interesting article on the differentiation of hyperparathyroidism and the milk-alkali syndrome.

To further confuse the picture, it is possible for chronic, long-standing kidney disease to produce secondary parathyroid hyperplasia, and chronic renal disease with insufficiency can occur as a secondary feature of primary hyperparathyroidism. And, finally, chronic renal disease and parathyroid adenoma or hyperplasia can develop as separate entities in the same individual.

Can we correlate the patient's chronic ulcer history with hyperparathyroidism? It has been reported in one series of patients with hyperparathyroidism that 24 per cent had clinical evidence of peptic ulcer at one time or another, and an additional 15 to 20 per cent of these patients had some ulcer-like symptoms without demonstrable x-ray evidence of ulcer. It was also stressed that peptic ulcers associated with hyperparathyroidism respond poorly to medical and surgical treatment until the hyperparathyroidism is cured, whereupon they become more amenable to therapy.

Our patient's chronic upper GI problems were not relieved by the gastrectomy carried out 15 years before the current admission. At the time of her gastric surgery, she had chronic bone changes in the spine and pelvis and probable calcinosis of the right kidney area which I believe can be interpreted as evidences of parathyroid disease. I shall try to support the diag-

nosis of adenoma of the parathyroid and chronic glomerulonephritis with renal insufficiency.

I believe that the osseous changes could be explained on either a renal or parathyroid basis. Renal insufficiency of long standing may lead to abnormal changes in the bone that cannot be distinguished roentgenologically from those caused by primary hyperparathyroidism. This type of renal disease with disturbance of the bone is best referred to as renal osteodystrophy. Any condition which leads to glomerular insufficiency will cause this condition.

Patients with primary hyperparathyroidism often develop renal damage as a result of excessive excretion of calcium, and ultimately this causes such damage to the kidney that phosphorus is retained in the serum. When this complication of primary hyperparathyroidism occurs, it is often difficult to distinguish primary hyperparathyroidism with secondary renal damage from renal osteodystrophy with secondary hyperparathyroidism. It is important, however, that the differential diagnosis be made if at all possible, since operation is mandatory in cases of primary hyperparathyroidism, whereas an operation would be not only useless but harmful in cases of renal osteodystrophy. Characteristic x-ray changes in either case are subperiosteal resorption of bone, loss of lamina dura, accompanied by other changes around teeth, and granular decalcification of the calvarium. The protocol does not report any x-rays of the hands or skull. Changes in the appearance of the vertebrae are not constant but in some cases the trabeculae are reported as appearing unusually coarse and prominent. The loss of the lamina dura strongly supports the diagnosis of hyperparathyroidism, although it is also seen in early Paget's disease and osteomalacia.

I conclude this patient has had a chronic nephritis of 30 years' standing which has been progressive with increasing evidences of renal insufficiency. I believe that she also has a hyperparathyroidism due to an adenoma of the parathyroid, that this disease process is of long standing and probably explains the failure of satisfactory clinical response to both medical and surgical management of her peptic ulcer. It is to be emphasized that she had chronic bone changes consistent with either hyperparathyroidism or renal osteodystrophy as long as 15 years prior to the current admission. I believe the

surgery was a neck exploratory procedure and that an adenoma or adenomas of the parathyroid were found. I further believe this patient's prognosis to be poor because of the severe kidney disease.

DIAGNOSES:

- (1) Hyperparathyroidism due to parathyroid adenoma.
- (2) Chronic glomerulonephritis with marked renal insufficiency.
- (3) Advanced calcinosis and osteodystrophy due to both kidney and parathyroid disease.
- (4) Hypertension with cardiac enlargement.

ROGER WHITE, M.D.

The case for discussion today is certainly a most interesting and challenging one; however, I must admit at the start that despite a great deal of extensive reading on probably a number of completely unrelated subjects, I feel no more sure of my answer after this investigation than I did after having read the first paragraph of the protocol for the first time.

The case is essentially that of a woman with a chronic nephritis, a long history of epigastric distress and upper gastrointestinal dysfunction, generalized pruritis and some indirect evidence of abnormal calcium, phosphorus and uric acid metabolism. We have a few positive laboratory and physical findings which will be found to be present singly or in combination with other factors in each of the clinical entities we discussed; however, it is quite obvious that all of these can fit only one clinical entity and that is my job—to find that one.

We have, No. 1, metastatic calcification or evidence of it as by the x-ray report of punctate calcification seen to the right of the first lumbar vertebra. This metastatic calcification can be found in hyperparathyroidism, hypervitaminosis D, renal rickets, renal osteitis fibrosa and, less commonly, in multiple myeloma; myelogenous leukemia, extensive skeletal metastases and in marble bone disease, to mention a few. The x-ray report of a dense granular appearance of the bones of the spine and pelvis can be found also in any of the above-mentioned clinical entities. Another striking and persistent feature of the latter part of the clinical course is the markedly elevated alkaline phosphatase activity. This reached a very high level at the time the protocol came to a close.

Serum phosphatase activity is consistently in-

creased in active rickets. High values, 15 to 125 units, are obtained rather consistently in polyostotic forms of Paget's disease. Normal or only slightly increased activity may occur in cases of localized involvement of one or two bones. Slightly elevated values, five to 15 units, have been reported occasionally in patients with osteoporosis, marked hyperthyroidism, osteomalacia, metastatic carcinoma, osteogenic sarcoma, Hodgkin's disease, lymphosarcoma with bone involvement, polyostotic fibrous dysplasia, Gaucher's disease, marble bone disease and, rarely, in renal rickets and multiple myeloma. Serum phosphatase activity is increased in a large portion of patients with obstructive and hepatocellular types of jaundice, levels rising to as high as 60 units. However, it seems to me that evidence of hepatic disease has been very clearly ruled out in this case.

Urinary calcium and phosphorus excretion in this case are purportedly within normal limits. One would expect if this were a true hyperparathyroidism to find a marked increase in both urinary calcium and phosphorus output. The reported laboratory values for serum calcium and phosphorus are somewhat more difficult to interpret in the light of our thinking concerning the nature of this case. In a classical hyperparathyroidism one should find a markedly elevated serum phosphorus and a markedly reduced serum calcium; however, as the disease progresses with progressive renal dysfunction, which is an inescapable part of chronic hyperparathyroidism, serum calcium levels may rise to near normal or low normal levels, and serum phosphorus levels may fall to normal or high normal.

This brief discussion of these laboratory characteristics that typify the clinical entities discussed above seems to me to be commonly applicable to only two conditions. Number one, primary hyperparathyroidism and, two, chronic glomerulonephritis.

I will first discuss hyperparathyroidism as a possible cause of this woman's difficulty. The skeletal lesions of hyperparathyroidism vary considerably and include generalized demineralization, multiple foci of osteitis fibrosa, single or multilocular cysts, hemorrhages, cortical thinning and localized expansion of the bones leading to fracture and deformity. Changes also occur in other tissues. The majority result from the direct action of excessive amounts of parathyroid hormone or from precipitation of calcium phosphate.

Degenerative changes may be found in the renal tubular epithelium, heart muscle, in gastric mucosa. Calcific deposits, probably erroneously termed metastatic calcification, may occur in these situations and also in the lungs and the walls of the arteries. Serious pathological changes in the kidneys are perhaps the most common of the extra skeletal lesions, occurring in about 50 per cent of the cases.

Clinical features can be briefly outlined as follows: About 70 per cent of the reported cases have been in women. The condition occurs most commonly between the ages of 20 and 60 years. Anorexia and constipation are often troublesome features due, probably, to the existing hypercalcemia. There may be periodic, recurring bouts of nausea and vomiting, at times a severe abdominal pain, these attacks usually lasting for a few days to two weeks. Urinary tract symptoms include polyuria, polydypsia, frequency of urination, enuresis, nocturia, dysuria, renal colic, pyeuria, and other manifestations of stone in the urinary passages, or renal failure. Renal complications have been reported in 30 to 70 per cent of cases of hyperparathyroidism. Miscellaneous symptoms include lassitude and muscular weakness, probably dependent upon muscular hypotonia due to hypercalcemia. Loss of appetite and loss of weight are nearly always present and may lead to profound emaciation. There may be extreme dehydration and a base deficit as a result of prolonged polyuria and a loss of sodium and other electrolytes in the urine. Respiratory difficulty and reduction in height may result in deformities of the thorax (kyphosis and scoliosis) due to softening and fractures. The metabolic manifestations of hyperparathyroidism have been discussed.

Although not specific for hyperparathyroidism, two findings noted in this case are frequently found. One, a white deposit in the paralimbal regions of both corneas on ophthalmologic examination and the loss of the lamina dura on the dental films. The other clinical entity that deserves equally serious consideration is chronic glomerulonephritis. This woman's bad obstetric history and apparent long-standing history of chronic nephritis indicates that she had a relatively marked degree of renal dysfunction dating back many years, perhaps many years prior to the date of the beginning of this protocol. Hypocalcemia is occasionally observed in non-nephrotic

forms of chronic glomerulonephritis in the stage of renal functional failure. It occurs usually in the late stages of this condition and is associated with and perhaps dependent upon the increase in the serum phosphorus which is present in such cases. The concentration of calcium varies inversely with that of phosphorus. Values as low as 4 to 6 milligrams have been observed occasionally. In many cases, the decrease in serum calcium is contributed to by the presence of hyperproteinemia which certainly was not the case in this protocol. It is believed by some that hypocalcemia may be responsible for certain of the manifestations of uremia. Chemical changes may occur in chronic nephritis or in the congenital urinary tract defects, their character varying from generalized osteoporosis to cyst formation and deformities with extensive metastatic calcification. Occurring during the period of skeletal growth, the condition has been termed renal rickets or renal dwarfism. A similar condition may occur in adults with fibrocystic changes in all bones and metastatic calcification, particularly in the media of the arteries, and in the neighborhood of the joints. This has been termed renal osteitis fibrosa cystica and is regarded as the adult counterpart of renal rickets. In both forms there are evidences of long-existing renal failure, usually marked acidosis, hyperphosphatemia, usually normal or slightly reduced serum calcium concentration, and generally normal serum phosphatase activity.

Parathyroid hyperplasia has been found in a large proportion of such cases, being probably compensatory in nature and induced by the prolonged increase in serum phosphorus. All the parathyroid glands are increased in size when hyperplasia is present. The nature and extent of the skeletal changes are not directly proportionate to the degree of hyperplasia, indeed may be marked in the absence of the latter, suggesting that the bone lesions are not caused by hyperparathyroidism in such cases. It appears probable that the bone changes are dependent primarily upon the effects of (a) acidosis and (b) inadequate absorption of calcium resulting from the excretion into the intestine of large amounts of phosphorus which would have been eliminated in the urine under conditions of normal renal function. Differentiation of this condition from hyperparathyroidism may be very difficult. Renal rickets may present all of the cardinal clinical and laboratory features of hyperparathyroid-

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references: 1. Strub, I. H.: Personal communication. 2. Ayd, F. J., Jr.: presented at Ohio Assembly of General Practice, 7th Annual Scientific Assembly, Columbus, September 18-19, 1957.



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ism, complicated by renal functional impairment. It usually differs in the following respects. (1) The renal impairment antedates the bone changes and frequently there is a long history of renal disease, often with hypertension and its attendant cardiovascular manifestations. If the onset occurs in early childhood, growth may be stunted. (2) The underlying cause is usually chronic glomerulonephritis, chronic pyelonephritis, or renal hypogenesis. Consequently, urinary lithiasis or nephrocalcinosis is rare in this condition, whereas they constitute a common basis for the development of advanced renal functional impairment in hyperparathyroidism. A good many clinical and laboratory observations have obviously been wilfully left from this protocol. Among them, however, the most valuable note would have been whether the operation performed was in the neck or below the diaphragm. Of course, that would be giving the whole thing away. We were faced then with making a choice in this case as to whether this was the case of primary hyperparathyroidism with attendant nephrocalcinosis and progressive renal failure, or a case of chronic glomerulonephritis of long standing with some evidence of parathyroid hyperplasia and hyperfunction. Inasmuch as we were obligated to commit ourselves as strictly as possible to one single diagnosis, I will say that this patient had primary hyperparathyroidism of long standing with secondary chronic glomerulonephritis due to nephrocalcinosis and that the operation performed was for exploration and removal of a parathyroid adenoma or adenomata.

DIFFERENTIAL DIAGNOSIS:

DR. WILLIAM V. McDERMOTT JR.: This 58-year-old woman had evidence of progressive renal disease and had had in the past an intractable duodenal ulcer, treated by a subtotal gastrectomy, after which she had persistent, relatively mild gastrointestinal difficulties and intermittent but apparently increasing pruritus. On the last admission the most striking finding was the hypercalcemia. The reason I say that this is perhaps the most striking finding is that it may provide a link for the various symptoms that had bothered this woman over the years — the intractable duodenal ulcer, with the persistent gastrointestinal symptoms and the pruritus. Dr. Oliver Cope has stressed for a long time the connection of gastrointestinal symptoms with hyper-

parathyroidism, which was obviously suggested by the hypercalcemia. Dr. St. Goar has studied the series of patients with hyperparathyroidism at this hospital and at the Presbyterian Hospital in New York City and has found an incidence of active duodenal ulcers of slightly over 8 per cent in both series. He stressed, however, not the incidence of the duodenal ulcer, but the fact that in cases in which an adenoma of the parathyroid gland was removed, the duodenal ulcer promptly healed, whereas previously it had been intractable. Therefore, there is apparently a connection between the hyperparathyroidism and the duodenal ulcer.

The next point is the elevated alkaline phosphatase. In the absence of disease of the liver or of the biliary tract, of which there was no evidence, this suggests the presence of osteoblastic activity. Perhaps, this would be a good time to look at the x-ray films, particularly of the bones.

DR. JACK R. DREYFUSS: This film from a gastrointestinal examination done 15 years before the present admission shows fairly normal bone structure and density. The small areas of intra-abdominal calcification that were described in the protocol are already present. The films taken on admission reveal a striking change in the appearance of the bones. The vertical height of the vertebrae is decreased, a scoliosis has developed, and the bone has a nondescript, coarse appearance, with areas that look decalcified. Films of the legs demonstrate a marked degree of arteriosclerosis, even for a patient of this age. Fluoroscopic studies were carried out to determine whether or not there was a parathyroid adenoma, but the only positive finding was a constant bulge of soft tissue just to the right of the suprasternal notch. We thought that this bulge was a vascular shadow in the mediastinum and not a true tumor. Other films were taken; I can show them after the conclusion of the discussion.

DR. McDERMOTT: Do you see a cyst anywhere?

DR. DREYFUSS: No; there are none. This is very peculiar bone; there are some areas of excess calcification, but mostly there is decalcification. The lamina dura of the teeth is definitely absent.

DR. McDERMOTT: Do you think that there was nephrocalcinosis?

DR. DREYFUSS: No; I think the calcifications, if anything, are small stones within the renal calyces.

DR. McDERMOTT: Do you think that this is consistent with osteitis fibrosa generalisata?

DR. DREYFUSS: Yes.

DR. McDERMOTT: There was, then, a pattern of diffuse bone disease, renal disease, duodenal ulcer, hypercalcemia and other findings. These bring to mind three main conditions: primary hyperparathyroidism, with secondary renal disease; primary renal disease, with secondary hyperparathyroidism; and the milk-alkali syndrome. The last was described by Burnett et al., and there is still some dispute over whether or not it exists as a separate entity, but since at the moment it is accepted as a clinical diagnosis and since it presents somewhat characteristic findings that fit this general pattern, I shall include it in the differential diagnosis. I shall not discuss other conditions associated with hypercalcemia because they seem so unlikely.

First, I should like to eliminate the so-called milk-alkali syndrome as a diagnosis. The reason for doing this is that the metabolic acidosis, although mild, which this woman had during the last admission, is actually incompatible with the concept of the development of the milk-alkali syndrome. If one postulates that she was in a phase of completely irreversible renal disease, I suppose that at a certain point it would be possible for her to have a metabolic acidosis. A specific point in the differentiation of this syndrome—improvement on a diet low in calcium and absorbable alkali—was not brought out in the case history, but that is another point against the milk-alkali syndrome.

Having eliminated the milk-alkali syndrome, I shall have to decide between primary hyperparathyroidism with renal disease and primary renal disease with secondary hyperparathyroidism. The confusion that exists in differentiating these two is caused by the fact that the renal insufficiency leads to a phosphorus retention, which in turn lowers the serum calcium and produces a compensatory hyperplasia of the parathyroid glands. This does not seem applicable, however, in this particular case. In the first place, the acidosis was mild, secondly, the excretion of phosphorus was normal or slightly elevated and, thirdly, the serum calcium was high. Although no one of these findings could serve to rule out renal disease, this combination makes that unlikely. The paralimbal calcifications, which were mentioned in the protocol, have been described

with hyperparathyroidism by Cogan, Albright and Bartter. They are not specific for this disease, but are found with hypercalcemia of any cause whatsoever.

In the differential diagnosis, the final step would be to eliminate hyperparathyroidism on the basis of the subnormal urinary calcium excretion and the high serum phosphorus. That is not practical because that would leave me without a diagnosis. Moreover, that is not compatible with the ground rules that Dr. Castleman has. Perhaps I can fit this picture into primary hyperparathyroidism and explain some of the apparent discrepancies. We know that primary hyperparathyroidism, if it continues sporadically over years, is attended ultimately by progressive renal disease, which in its extreme manifestation is attended by an elevation in the serum phosphorus, and, at a certain stage in renal insufficiency, the excretion of calcium in the urine, which is commonly high with hyperparathyroidism, may actually be lower than normal. To carry this thesis further, I wonder whether, if this diagnosis had been made 15 years before admission and a parathyroid adenoma had been removed, the patient would have been spared the subtotal gastrectomy and the renal insufficiency. My final diagnosis is a parathyroid adenoma with secondary renal insufficiency and osteitis fibrosa generalisata.

DR. ANNE P. FORBES: I should like to say that by the time there is an elevation of the non-protein nitrogen with primary hyperparathyroidism there may also be a high serum phosphorus. To back Dr. McDermott up in excluding the milk-alkali syndrome, I shall point out that the phosphatase would not have been high at this stage in that syndrome.

DR. WALTER T. ST. GOAR: I should also like to support Dr. McDermott's diagnosis. The x-ray films that have been shown, including those of the lamina dura, cannot be said to be pathognomonic of hyperparathyroidism, although taken together they are highly suggestive. Further x-ray films of this patient's hands show the typical subperiosteal reabsorption of bone that is said to be pathognomonic of increased parathyroid activity. The fact that she had an elevated serum calcium level excludes secondary hyperparathyroidism, and thus, even in the presence of the elevated serum phosphorus level, one can make a diagnosis of primary hyperparathyroid-

ism on the basis of hypercalcemia, together with x-ray films of the hands. Perhaps Dr. Dreyfuss will show us those films.

DR. DREYFUSS: The film of the skull demonstrates definite increase in the thickness of both tables. At first glance it almost looks as though there were areas of increased calcification. I think, however, that we are seeing a reflection of spotty decalcification. The films of the hands are almost diagnostic. There has been resorption of the ungual tufts and subperiosteal decalcification along the phalanges.

CLINICAL DIAGNOSIS:

Hyperparathyroidism.

Dr. William V. McDermott Jr's Diagnoses:

Parathyroid adenoma, with hyperparathyroidism and progressive renal disease.

Osteitis fibrosa generalisata.

ANATOMICAL DIAGNOSES:

Parathyroid adenoma

(Hyperparathyroidism)

(Peptic ulcer.)

PATHOLOGICAL DISCUSSION:

DR. BENJAMIN CASTLEMAN: At operation, Dr. Oliver Cope found a parathyroid tumor in the lower right side that extended into the anterior mediastinum. The tumor weighed over 12 gm., which is very large. One would expect a large tumor if the hyperparathyroidism with bone change had been present since the ulcer symptoms occurred 15 years before admission. Cross-section of it revealed the characteristic orange-brown color of the parathyroid tissue. This tumor did have large numbers of cysts in it, and this is also a common finding in parathyroid adenoma. Microscopically, the tumor contained large chief cells and cystic degeneration.

DR. DREYFUSS: In retrospect, I think from the size of the lesion and its location, I can say that the bulge that we thought was vascular is probably the adenoma. The pulsation that we noted must have been transmitted.

DR. CASTLEMAN: In the Johns Hopkins Hospital series, 15 per cent of the patients with hyperparathyroidism had ulcer. Hellstrom, in Sweden, reported a 14 per cent incidence. It is believed that one of the causes of the ulcer is deposition of calcium in the gastric mucosa, which in turn leads to ulceration. In most of our cases of hyperparathyroidism in which we have

examined the stomach, we have not found any foci of calcification. This brings up the question of whether every patient with peptic ulcer should have serum calcium and phosphorus determinations. Dr. Culver, what would you say about that?

DR. PERRY CULVER: Dr. St. Goar has done a good job by calling our attention to this, but we do not want to let our enthusiasm run away. I should think that in any case resistant to therapy, one would consider hyperparathyroidism and obtain calcium and phosphorus determinations. We are not justified in spending that much money on every patient with an ulcer, however.

DR. BERNARD M. JACOBSON: What is the percentage of hyperparathyroidism in ulcer?

DR. ST. GOAR: It is not very great.

I should agree with Dr. Culver. When a peptic ulcer is present in a patient with hyperparathyroidism, there are almost always other signs or symptoms that, if recognized, will suggest the possibility of a parathyroid adenoma. I should look on an ulcer and other unexplained gastrointestinal symptoms only as clues for exploring symptoms referable to the renal tract and skeleton, which are apt to give more specific evidence for or against the presence of hyperparathyroidism. What seems important is to make an early diagnosis of this disease, which is correctable if caught at an early stage but which may, if not recognized early in its course, go on to skeletal deformity and irreversible renal damage. It would seem to be a good idea to do calcium and phosphorus determinations on any patient with a peptic ulcer who has reached the point where surgery is planned.

DR. FORBES: Those determinations should certainly be done in such patients if they have abnormal urinary findings. This patient had unexplained albuminuria and already some signs of renal damage.

DR. CASTLEMAN: At the time of the two pregnancies you mean?

DR. FORBES: Yes.

DR. McDERMOTT: Perhaps we should stress the appearance of a duodenal ulcer in a female, which might be a greater diagnostic indication of hyperparathyroidism than it would be in a male.

DR. EDWARD D. CHURCHILL: Do you not think it might be as dangerous to keep a patient on a high milk (high-calcium) diet year after year as it would be to do a subtotal gas-

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trectomy? Such a diet is not very good for the kidneys in the presence of hyperparathyroidism. What is the present opinion on that?

DR. ST. GOAR: The milk-alkali syndrome does not develop in many patients with chronic duodenal ulcer who are treated medically. I wonder if Dr. Forbes and Dr. Moldawer will support my impression that it is usually only patients with renal disease who acquire this syndrome.

DR. MARC P. MOLDAWER: I do not believe we have seen a serum calcium greater than that normal in the secondary hyperparathyroidism of renal failure per se. A high serum calcium in the presence of an elevated nonprotein nitrogen, therefore, should suggest that hyperparathyroidism has been the cause of the renal failure. It is somewhat surprising to find bone disease in this patient, in that in general a high-calcium intake in hyperparathyroidism is protection against osteitis fibrosa.

DR. MARIAN W. ROPES: I agree that the other signs of involvement and the other symptoms are more important than the gastrointestinal symptoms. I think that the urine showed enough change 15 years before admission to have warranted consideration of hyperparathyroidism.

A PHYSICIAN: If this patient had been on the urological service, since she had a stone, a calcium and a phosphorus determination would have been done.

DR. CASTLEMAN: Yes; I think that the urologists have found that 5 to 8 per cent of patients with renal stones have hyperparathyroidism.

DR. ST. GOAR: I think that percentage is too high. The figures on the incidence of hyperparathyroidism in patients with renal stones have come from series of patients in large diagnostic centers and I suspect that the frequency of hyperparathyroidism has been slightly exaggerated. (These reports have ranged from 3 to 10 per cent.) I looked through 350 cases of renal stones at the Queen Elizabeth Hospital in Birmingham, England, last year and was able to find only two cases of hyperparathyroidism. It is true that serum chemical determinations were not available in about 25 per cent of these cases, but I had access to the clinical records.

A PHYSICIAN: What is thought about the intravenous calcium-tolerance test?

DR. FORBES: I think the patient was carrying out her own intravenous calcium-tolerance

test. The fact that she had a high serum calcium and no calcium in the urine might be added evidence for renal damage.

DR. ST. GOAR: The calcium-infusion test requires a large number of chemical determinations, making it expensive to carry out, and furthermore to evaluate its results in the presence of renal disease is difficult, if not impossible.

DR. CASTLEMAN: Dr. Barnes, will you tell us about the postoperative course?

DR. BENJAMIN A. BARNES: Postoperatively, the patient was unusually refractory to calcium therapy. She received large doses of calcium orally and of calcium gluconate both intravenously and intramuscularly. About six weeks elapsed before the serum calcium stabilized to the level that permitted her to leave the hospital. Usually, the serum calcium rises from tetanic levels in two weeks or less.

DR. CASTLEMAN: Do you mean that she was in tetany most of the time?

DR. BARNES: She had a prolonged period of adjustment, during which a positive Chvostek sign was present, as were intermittent attacks of diarrhea associated with abdominal cramps. The serum calcium had only increased to 7 mg. per 100 ml. at the time of discharge. It had been as low as 5 mg. per 100 ml. on the seventh postoperative day.

DR. CASTLEMAN: Dr. Cogan, do you have a comment about the hypercalcemia and the paralytic calcifications?

DR. DAVID G. COGAN: I should like to emphasize the fact that it is a sign of non-specific hypercalcemia.

DR. JOHN A. BENSON JR.: One of the questions bearing on the prognosis was how much secondary hyperparathyroidism had been induced and therefore how much renal improvement we could expect after the removal of the adenoma. Was another parathyroid gland biopsied?

DR. CASTLEMAN: Dr. Cope took a biopsy of one of the other glands; it showed normal activity; it was not atrophic. Whether that was an indication of mild secondary hyperplasia of the other glands, I cannot say.

DR. ST. GOAR: The postoperative course suggests that the parathyroid glands were not working up to even normal activity. Theoretically, the high level of serum calcium before operation would have tended to suppress the

activity of the three normal parathyroid glands — that is, of course, if the level of serum calcium is the thermostat regulating parathyroid function.

DR. BARNES: The important point for the future is whether a reversal in the chronic renal damage will take place or not. We do not have too much evidence about this aspect of the convalescence in patients with chronic nephritis.

DR. FORBES: I have seen improvement in kidney function after removal of a parathyroid adenoma, even when the patient was already in mild uremia.

DR. BARNES: It is too early to obtain such evidence in this patient.

DR. CASTLEMAN: You do know, Dr. St. Goar, that the ulcer symptoms really disappear

after the removal of the parathyroid gland?

DR. ST. GOAR: There were seven patients in the Presbyterian Hospital series with a non-protein nitrogen over 40 mg. per 100 ml. at the time of parathyroidectomy. Three of these seven patients went into progressive renal failure after operation. Two were well, with normal non-protein nitrogen levels, seven and eight years after operation. Two have not had sufficient follow-up study for any conclusions to be drawn. Three had elevated serum phosphorus levels at the time of operation, which were explained on the basis of renal insufficiency. Two of these patients died two years, and the third four years after parathyroidectomy, all from renal failure. Thus, an elevated serum phosphorus at the time of operation is probably a poor prognostic sign.

T AMERICAN CANCER SEMINAR

THE AMERICAN Cancer Seminar sponsored by the Arizona Division of the American Society held in Tucson late in January of 1958 presented an excellent program and was well attended. It is interesting to note that 17 states other than Arizona were represented at this meeting by 49 doctors.

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AMERICAN MEDICAL EDUCATION FOUNDATION

THE AMERICAN Medical Education Foundation, sponsored by the American Medical Association was organized in 1951 to solicit funds for the medical schools from members of the medical profession. It is dedicated to the private support of medical education in our nation. The contributions assure us that the medical schools will continue to maintain their high standards by providing yearly grants to these schools. The American Medical Education Foundation has raised more than \$4.6 million for our medical schools since 1951.

In 1949, business leaders organized the National Fund for Medical Education to solicit contributions from business and industry and they play a very large part in this very vital work. The funds of these two foundations are combined into one general fund and in turn is distributed among all medical schools.

Our nation's 81 medical schools need \$10 million annually in additional income in order to maintain the present high teaching standards in the training of physicians, also to carry on the vast amount of research which has produced such gratifying results in the past few years. Tuition to these medical schools has increased greatly in the past 15 years it is true but this pays only about one-fifth of the cost of a medical education provided by these schools. The rest

must be provided by other means: gifts, grants etc. The medical schools are doing a wonderful work on the nation's health program and they, in turn, must receive the financial support they need.

One of the very important projects of our medical auxiliary is to stress the very vital importance of the work of the AMEF and its importance to the freedom of medicine through voluntary support as against socialized medicine through federal control.

We of the auxiliary have many ways in which we may be of much assistance in this project for our medical schools. In the year 1956-1957 the auxiliary turned in \$113,540 to this fund. The national goal this year is \$150,000. It is the privilege of each doctor's wife to help in this very worthwhile campaign.

The auxiliary employs several ways for raising funds namely: Sympathy and memorial cards, In Appreciation cards, gift cards, Christmas cards, teas etc.

The health of our nation is dependent upon our medical schools for from their classrooms come our doctors, nurses and others of this profession who so ably serve the health of our country. The standards can never be lowered, so we can readily see the magnitude of this task at the same time recognizing our duty and privilege of helping.

MRS. HENRY A. HOUGH,
State AMEF Chairman

AN INVITATION TO CONVENTION

I WISH to extend a cordial invitation to every doctor's wife in Arizona to attend the 28th annual convention of the Women's Auxiliary to the Arizona Medical Association which is to be held at the San Marcos Hotel, Chandler, April 30, and May 1, 2, and 3.

Mrs. Thomas Rowley (Barbara) of Mesa will be your convention chairman, assisted by the hostess auxiliary, Maricopa County.

We realize that this is a time away from the tasks of daily routine and the convention committees have given much time and thought to make this gathering one of enjoyment as well

as education.

It will be our privilege to have our national president, Mrs. Paul C. Craig of Wyomissing, Pa., as our honored guest.

I hope that you will plan to come to the convention to share with us the programs and social events that have been planned for you.

I shall look forward to the pleasure of greeting all of you at Chandler.

Sincerely,

MARJORIE I. POWELL
(Mrs. Charles S.)